Chapter 5
Cultivation and Utilization of *Valeriana jatamansi* Jones for Conservation Planning and Management

Arun Kumar Jugran, Indra D. Bhatt, and Ranbeer S. Rawal

Abstract *Valeriana jatamansi* is a medicinal herb generally known as Indian Valerian belongs to family Caprifoliaceae. This is an herbal plant blended with many medicinal properties such as stimulant, carminative, antispasmodic, cytotoxic and aromatic property. The herb is used in custom and advanced medicine system for curing various ailments and in flavor and perfume industries. In this study, brief phytochemical, traditional and pharmacological studies of species and prospects of the species in future are envisaged. This study also evaluated domestication and cultivation practices available on *V. jatamansi*. Six major groups of active constituents, namely valepotriates (145), lignans compound (18), flavones or its glycosides (18), sesquiterpenoids or its glycoside (12), bakkenolide-type sesquiterpenoids (6), phenolic constituents (6), miscellaneous compounds (12) and major oil constituents (294) have been listed from *V. jatamansi*. Several therapeutic properties, e.g., neurotoxic, cytotoxic, sedative, anti-inflammation, antidepressant, antidiarrheal, anti-HCV, adaptogenic, analgesic, antioxidant and antimicrobial effects and key compounds responsible for these properties have been described. The present study clearly indicated that this plant comprises huge potential for future research and drug development. Numerous active constituents discussed in the present study can be vital for further in vivo and in vitro experimentation. The study suggested the need to promote research on identification of active component from the species and their mechanism of action. Methods available for cultivation and domestication of *V. jatamansi* will be applicable for multiplication of this valuable species to meet out domestic and industrial demand. Findings from the study will be useful for conservation planning and sustainable uses of this valuable species.

Keywords *Valeriana jatamansi* · Ethnopharmacology · Phytochemistry · Active constituents · Domestication · Cultivation

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Abbreviations

2,4-D	2, 4-dichlorophenoxyacetic acid
Azoto	Azotobacter
BA	Benzyl adenine
DW	Dry weight
IHR	Indian Himalayan Region
FYM	Farm yard manure
GABA	Gamma Aminobutyric Acid
IAA	Indole-acetic acid
IBA	Indole-3-butyric acid
MAPs	Medicinal and Aromatic Plant
NAA	α-naphthalene acetic acid
PSB	Phosphate Solubilizing Bacteria
VAM	Vesicular-Arbuscular Mycorrhiza

5.1 Introduction

Valeriana jatamansi (Indian Valerian or Tagar) is an herbaceous plant of family Caprifoliaceae used for treatment of several ailments. Various active constituents like valepotriates (iridoids) are the major active component of this herb which comprises several properties like anticancer, anti-inflammatory, hepatoprotective, anticoagulant, antioxidative, antibacterial, antifungal, antiprotozoal and neuroprotective (Dinda et al. 2009; Jugran et al. 2019). The uses of *V. jatamansi* are mentioned in Charaka Samhita, Rigveda, and modern medicine system. The most of the demand for the species is generally fulfilled from wild by harvesting its natural populations which has resulted into a huge pressure on the natural habitats/populations. Therefore, there is the need of use species sustainably for its conservation in present as well as in future. Cultivation of medicinal plants is a vital procedure applied to conserve the medicinal plants under endangered status. The cultivation of MAPs is helpful to meet out ever-increasing demand for material of a particular species without disturbing natural environment (IUCN 1993). Medicinal plants including *V. jatamansi* are harvested from wild, and only a few reports are available on the cultivation of this species. The studies have been attempted to cultivate *V. jatamansi* plants growing in wild conditions to semi-natural agroforestry system. However, proper agrotechniques required knowledge on ecology, adaptation and pollination, conditions on *V. jatamansi* before the cultivation and raising nursery. The species is mostly collected from its natural sources in wild which has imposed a huge pressure on their natural habitats. Therefore, domestication of medicinal plant for conservation is a viable option, but quality of a species depends mainly on the amount of effective constituents present in a species. Hence, determination of phytochemicals for selecting elite genotypes/individuals/populations is immediately needed.

Studies demonstrated that quality and consistency of the secondary metabolites in wild and field grown plants of a species are varied (Bhatt et al. 2012). Similarly, habitat and altitude also impact the quality of the active principals and genetic diversity of this valuable species (Jugran et al. 2013a, 2015a, 2016a, 2018). This finally impacts the market and economic returns of a valuable species. Hence, identification of elites and development of appropriate, cultivation packages will be highly beneficial for prioritization and planning conservation strategies of such species especially for successful reestablishment in wild. Once, elite plants/populations are identified conventional and modern tools can be attempted for large-scale multiplication of high yielding individual/population to obtain quality material for planting. However, in vitro methods of propagation using shoot tip and axillary bud explants of *V. jatamansi* have been employed to develop and raised plantlet which then effectively shifted to the field plots for adaptation (Mathur et al. 1988; Mathur and Ahuja 1991). Likewise, Purohit et al. (2015) developed methods for proliferation of *V. jatamansi* by explant collected from leaf. Moreover, further improvement in these protocols is required. Keeping this background in mind, the present study is attempted.

5.2 Geographic Distribution

V. jatamansi is a high-value perennial medicinal plant widely distributed in India, Burma, Bhutan, China, Nepal and Afghanistan (Polunin and Stainton 1987; Jugran et al. 2013a). The species grow in varied habitat condition and demonstrated high adaptability toward diverse environmental conditions (Rather et al. 2011). Studies from Uttarakhand, a Western Himalayan state, reported that the species grows between 1000 and 3000 m asl (Jugran et al. 2013a, b, 2015a, b, c, 2016a). Another study revealed that this plant is distributed naturally Western Himalaya particularly under canopy of *Pinus roxburghii, Cedrus deodara, Quercus leucotrichophora* and grassy habitat and mixed forests habitat (Pande and Shukla 1993; Jugran et al. 2013a). *V. jatamansi* preferentially grow under sloppy, wet and humid places, ditches, soggy woods and alongside the streams. However, in the Eastern Himalaya *V. jatamansi* is observed to associate with *Castonopsis indica, Ficus nemoralis, Rhododendron arboreum* and *Ficus cordata,* ranging from 1290 to 2000 m (Mukherjee and Chakraborty 2014). Flowering and fruiting period for the species is March–June. Sexual (through seeds) and asexual (through rhizome) means of reproduction approaches are reported for this species. Pollination in *V. jatamansi* is affected by insects belonging to order Diptera and Hymenoptera (Khajuria et al. 2011; Jugran et al. 2018). *V. jatamansi* seeds are observed to be very small in size with feathery follicle and produced in large number. Further, stylar movement is a vital phenomenon in *V. jatamansi* which is helpful to maintain the survival and growth of the plant in harsh climatic condition (Khajuria et al. 2011). As no or little cultivation practices for the species are available, it is collected from wild at large scale which has resulted into overutilization and loss of habitats (Samant et al. 1998). However, cultivation practices for *V. jatamansi* species are started in Uttarakhand at the farmer

level in few village clusters (Phondani et al. 2016) but it was not attempted at larger scale till date. Moreover, above the altitude of 1800 m this species demonstrated low adaptability (Mukherjee 2015). Comparative analysis of these finding revealed an additional adaptability of the plants growing in Western Himalayan region then the eastern region. The reason of differences in adaptation can be associated with the variations in climatic situations.

5.3 Brief Phytochemistry of *V. jatamansi*

Numerous compounds obtained from *V. jatamansi* are belonging to family of phenolics, flavonoids, iridoids, bakenolloids, etc. as the major compounds. The dominant compound categories were valepotriates, linarines, bakkenollide and essential oils. Recently, Jugran et al. (2019) reported that 511 compounds were present in this species, of which 298 were oil components. The dominant constituents of *V. jatamansi* are linarin-isovalerianate (Thies 1968), valepotriates (Becker and Chavadeoi 1985), sesquiterpenoids (Ron et al. 2000), dihydrovaltrate (Bounthanh et al. 1981), hesperidin and 6-methylapigenin, etc. (Marder et al. 2003). Valepotriates are the major chemical constituents among them employed for several medicines. These are a group of monoterpenoids containing iridoid-type compound containing an epoxy group and β-acetoxy isovaleric acids. Iridoid compound extracted from Caprifoliaceae members is also known as valeriana-epoxy triesters, generally abbreviated as valepotriates for convenience (Thies and Funke 1966). Thies (1968) isolated the valeopotriates from *V. jatamansi* and named them as valtrate, acevaltrate and didrovaltrate. New acylated iridoids, jatamanvaltrates A-M were extracted from *V. jatamansi* recently (Lin et al. 2009). Xu et al. (2011a) isolated two bakkenollide-type sesquiterpenoids from this species. Likewise, valeriandoids A–C along with three known analogs were extracted from the *V jatamansi* roots (Xu et al. 2011b). Active components like valerianine, valerenic acid, valeranone, isovalerenic acid, 1-camphene, ar-cucumene, xanthorrizol, alpha-santalene, 1-pinene, terpineol, bornylisovalerinate, alkaloids, chatinine formate glucoside, etc. are also detected in rhizomes and roots oil of the species (Arora and Arora 1963; Nadkarni 1976; Bos et al. 1996; Rawat et al. 2017; Bhatt et al. 2012). Maaliol, citric acid, succinic acid, tartaric acid, and malic acid are also occurred in the rhizome of the species (Kapoor 1990). Valtrate, didrovaltrate, maaliol, 8-acetoxy patchouli alcohol and patchouli alcohol have also been recorded from *V. jatamansi* (Keochanthala-Bounthanh et al. 1993; Mathela et al. 2005). Besides, sesquiterpene hydrocarbons (ar-curcumene, α- and β-patchouolenes, β-fornesene and sesquifenchene) valerenone, cryptomeridiol, patchouli alcohol, etc. are determined (Houghton 1999).Valerenic acid was also estimated in the aerial and root parts of *V. jatamansi* (Singh et al. 2006; Jugran et al. 2016a) and considered as a marker compound which possess sedative and spasmolytic activity. An alkaloid valeranine is also derived from this species. The structures of few principle chemical

components obtained from the species are presented (Fig. 5.1). Likewise, details of major chemical methods used to detect dominant constituents from *V. jatamansi* are provided (Table 5.1).

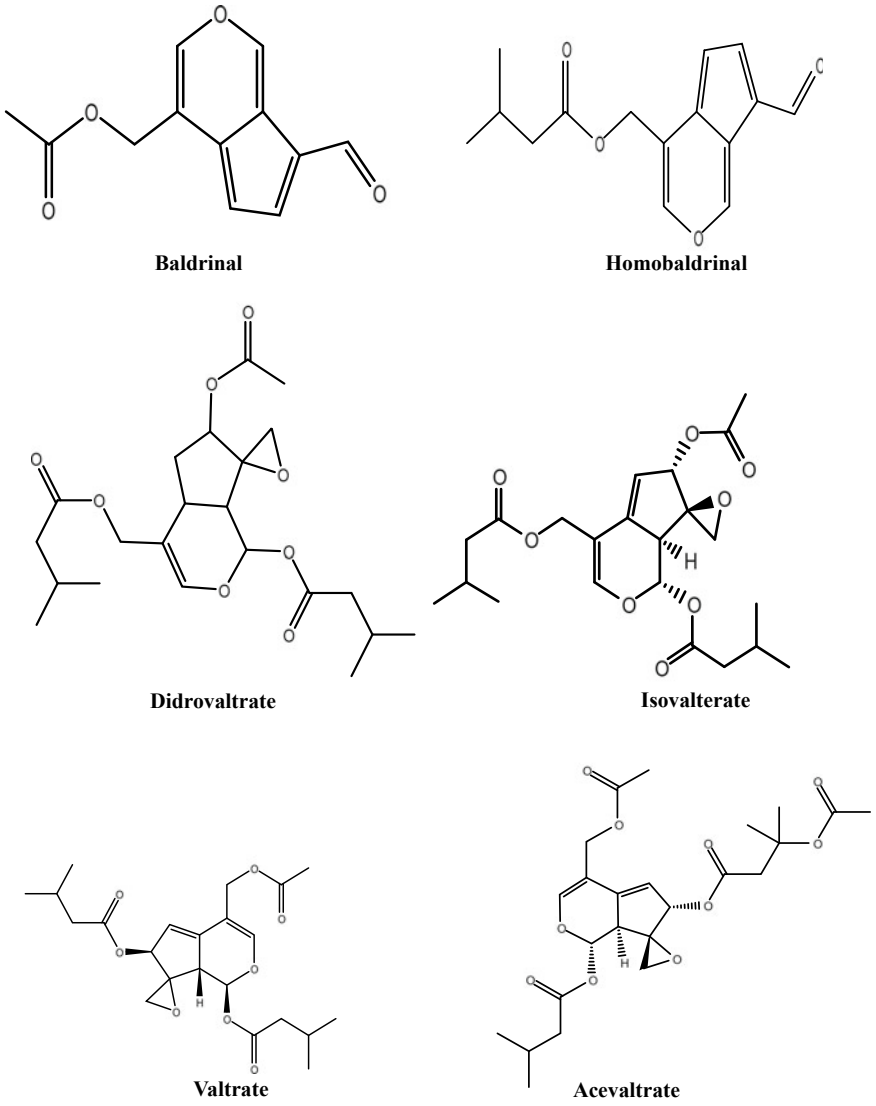
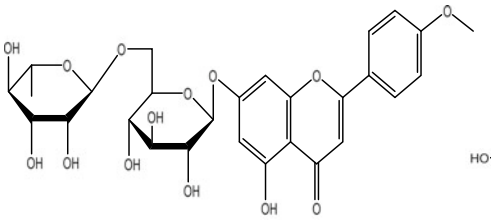
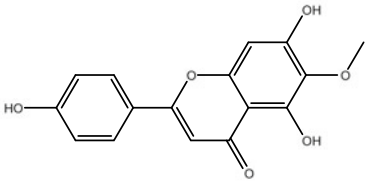


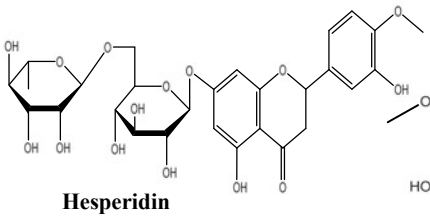
Fig. 5.1 Major active constituents reported from *V. jatamansi*



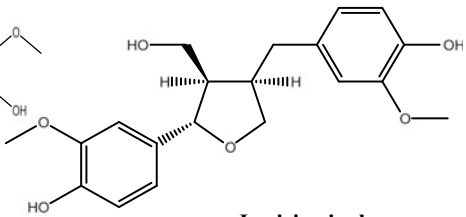
Linarin



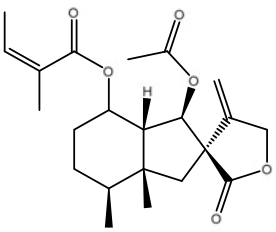
6- methylapigenin/Hispidulin



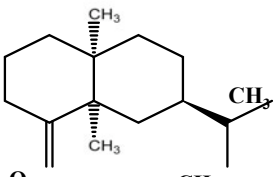
Hesperidin



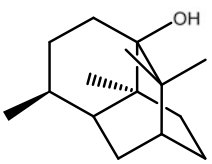
Lariciresinol



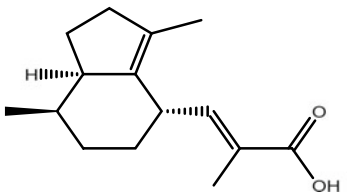
Bakkenolide B



Valeranone



Patchouli alcohol



Valerenic acid

Fig. 5.1 (continued)

Table 5.1 Chemical analysis of *Valeriana jatamansi*

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
1	HPLC-UV	a	Roots	Hesperidin	Dimethyl sulfoxide	Solution A; Water: O-phosphoric acid (99.7: 0.3) and Solution B; acetonitrile: methanol (75: 25)	Powdered root sample (100 g) was saturated in water (500 mL). Supernatants were pooled, filtered and consequently centrifuged. The collected supernatant was lyophilized, dried and stored at 5 °C for the further evaluation	Katoch et al. (2012)
		b	Aerial and root portions	Gallic acid, catechin, hydroxyl benzoic acid, caffeic acid, chlorogenic acid and coumaric acid	Methanol	Water: methanol: acetic acid	Dried powder (1.0 g) was mixed with 25 mL methanol, sonicated and centrifuged. Supernatants were collected, filtered and stored at 4 °C for analyses within 24 h	Bhatt et al. (2012), Jugran et al. (2015d)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
		c	Root and rhizome	Homoisovaltrate, 1-acevaltrate, isovaleroxyhydroxy didrovaltrate, didrovaltrate	Dichloromethane	Acetonitrile: water (80:20)	The dried plant material was subjected to dichloromethane extraction. The extract was concentrated on rotary evaporator to yield a brown dry mass	Sah et al. (2011)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
2	HPLC-PDA	a	Roots and rhizome	Chlorogenic acid, *massoniresinol*-4′-*O*-β-D-glucoside, berchemol-4′-*O*-β-D-glucoside, pinoresinol-4,4′-di-*O*-β-D-glucoside, 8-*hydroxypinoresinol*-4′-*O*-β-D-glucoside, pinoresinol- 4-*O*-βD-glucoside, hesperidin, linarin, hydroxyvalerenic acid, acetoxyvalerenic acid and valerenic acid	Methanol	Water and acetonitrile-methanol (1 + 1), both with 0.05% phosphoric acid	Dried powdered material (0.2 g) was sonicated in 2.5 mL methanol for 15 min. Centrifuged and supernatant was collected. The supernatants were pooled, and final volume was adjusted to 10 mL with methanol. All samples were diluted and filtered through a 0.45-μm nylon membrane filter prior to use	Navarrete et al. (2006)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
3	HPTLC	a	Rhizomes; aerial and root portion	Valerenic acid	Methanol	Hexane: ethyl acetate: acetic acid (75:25:0.5v/v)	The air-dried powdered material (0.2 gm) was extracted in 20 mL of methanol. The extracts were filtered, concentrated and dissolved in 2 mL of methanol	Singh et al. (2006), Jugran et al. (2016a)
		b	Rhizome	Hesperidin	Methanol	Ethyl acetate: methanol: water (10:1.7:1.3, v/v)	100 mg of the extract was dissolved in 2 mL of methanol. The mixture was sonicated, diluted and centrifuged. The supernatant was analyzed for hesperidin content	Sharma et al. (2012a)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
4	GC and GC-MS	a	Roots and rhizomes	Sesquiterpene hydrocarbon, α-santalene, ar-curcumene, xanthorrhizol, patchouli alcohol	Water	Nitrogen as a carrier gas	20 g of air-dried, freshly ground material or 10.0 g of dry and ground root material hydrodistilled for 4 h in 300 mL water. The oil samples were stored at − 20 °C until analyzed	Bos et al. (1997)
		b	Leaf and root	3-Methylvaleric acid, maaliol (leaf oil), maaliol, β-gurjunene (root oil)	Water	Helium as a carrier gas	Fresh leaves and roots were collected and subjected separately for steam distillation to obtain oil	Sati et al. (2005)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
		c	Roots and rhizomes	Patchouli alcohol, maaliol, isovaleric acid, viridiflorol (in rhizome oil), α-bulnesene, α-guaiene, bornyl acetate, 7-*epi*-α-selinene, γ-patchoulene and β-elemene (in root oil)	Water	Hydrogen as a carrier gas	Freshly harvested, cleaned and crushed rhizomes and roots separately hydrodistilled. The oil samples obtained were kept in a cool and dark place before analyses	Verma et al. (2013)
		d	Roots	Patchouli alcohol, maaliol, seychellene, calarene/s-gurjunene, α-santalene	Water	Helium as a carrier gas	Freshly harvested roots were air-dried in the shade at room temperature. The essential oil was extracted by hydrodistillation and stored at 4° till further analysis	Raina and Negi (2015)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
		e	Whole plants	3-Methylvaleric acid, maaliol and β-gurjunene	Water	Helium as a carrier gas	Fresh plant material was collected and hydrodistilled in a Clevenger to obtain essential oil	Irshad et al. (2012)
		f	Rhizome	Isovaleric acid, methylvaleric acid and seychellene	Chloroform	Helium as a carrier	Hydrodistillation of the rhizome using the clevenger-type apparatus. The essential oil was collected and stored at 4 °C until analysis	Pandian and Nagarajan (2015)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
		g	Roots	β-vatirenene, dehydro aromadendrene, alcohol, α-muurolene	Water	Helium as a carrier gas	Hydrodistillation of the roots using the clevenger-type apparatus. The oil was stored at 4 °C until evaluation	Thusoo et al. (2014)
		h	Roots and rhizome	Patchouli alcohol, seychellene, α-guaiene, α-humulene, δ-guaiene	Water	Helium as a carrier gas	Fresh roots (40–60 g) were hydrodistilled, and essential oil was dried through passing over anhydrous sodium sulfate. After filtration oil was stored at 4 °C till analysis	Bhatt et al. (2012)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
		i	Roots	Patchoulol, α-bulnesene, isovaleric acid, α -guaiene and 3-methylvaleric acid	Water	Helium as a carrier gas	Powdered sample was hydrodistilled and extracted with *n*-hexane. Anhydrous sodium sulfate was used to remove water. Essential oils were stored in a refrigerator at 4 °C for subsequent experiments	Liu et al. (2013)
		j	Rhizomes	Isovaleric acid, methylvaleric acid and seychellene	hydrodistillation and supercritical fluid CO_2 extraction	Helium was the carrier gas	Samples were hydrodistilled, and obtained essential oil was collected and stored at 4 °C until analysis	Pandian and Nagarajan (2015)

(continued)

Table 5.1 (continued)

S. No.	Method	Type	Part	Marker	Solvent	Mobile phase	Sample preparation	References
5	GC-FID and GC-MS	a	Whole plant	Carotol, germacrene B, cis-β-farnesene, α-humulene and humulene oxide	Water	Helium as a carrier	Plant material (500 g) was shade dried, coarsely powdered and hydrodistilled. The oil was dried over anhydrous sodium sulfate and stored at 4 °C in the dark	Agnihotri et al. (2011)

5.4 Medicinal Properties and Usage

5.4.1 Traditional Uses

V. jatamansi is a vital species used in traditional and modern medicines for its aromatic, stimulant, carminative and antispasmodic property. Various activities like anticoagulant, anticancer, hepatoprotective neuroprotective, antibacterial, antifungal, inflammatory, antioxidative and antiprotozoal are reported in naturally occurring valeopotriates/iridoid (Dinda et al. 2009). This herb as a single species or in polyherbal combination is used to prepare 39 Ayurvedic formulations (Jugran et al. 2019). *V. jatamansi* is utilized for the administration of hysteria, epilepsy and urinary disorders (Singh and Ali 1998; Sharma 2003) and for removing bad smell of mouth due to toothache (Jugran et al. 2019). In the situation of extreme headache, *Valeriana* leaves are scrubbed on forehead after crushing them (Bhattacharjee 2008; Chevallier 1999). Dried rhizomes of *V. jatamansi* are utilized for scents, blackening of hair and as an aroma (Bhattacharjee 2008). The species is beneficial for the administration of head, eye and diseases releted with blood, liver, spleen-associated diseases, kidney ulcers, cardiac weakness, wounds, dry cough, asthma, prolonged and irregular body temperature (Awan 1990; Prakash 1999). Additionally, *V. jatamansi* extract is also used for curing diseases of skin, obesity, nervousness, hysteria, failing impulses, insanity, neurosis, sciatica, tranquilizer, snake poisoning and emmenagogue (Nadkarni 1976; Baquar 1989). Diuretic (Said 1970) and hepatoprotective activities are also reported (Awan 1990). Clinical and animal trails exhibited the CNS depressant property of *V. jatamansi* (Marder et al. 2003). Flavor, medicinal and perfume productions utilized extract and essential oil derived from this plant particularly for flavoring honey, tobacco and root beer (Sah et al. 2010a). An iridoid ester called as jatamanvalterate P extracted from this plant conventionally used to cure nervous ailment (Yang et al. 2017). Traditionally, several herbal formulations of the *V. jatamansi* plant are orally supplemented for curing diarrhea (Awan 1990), hypertension (Chevallier 1996) and gastrospasms (Kapoor 1990). Nadkarni (1976) reported that *V. jatamansi* is used in inflammation like jaundice and scorpion stings.

5.4.2 Pharmacological Activities

Several studies have been conducted to investigate the pharmacological attributes of *V. jatamansi*. Numerous active components extracted from this herb exhibited different level of activities to decrease stress and nervous disorders. Bhattacharya et al. (2007) reported that *V. jatamansi* extract also attenuated anxiety, stress and depression. The extract of species is useful in cerebro-spinal coordination, and migraines, nervous unrest, wakefulness, health obsessiveness, neuralgia and neuroasthemia were also observed (Cionga 1961). Depressed CNS activity is observed using the species extract in mice when supplemented orally (Veith et al. 1986). Neurotropic

activity of valiracyl derived from the species increases the amount of mediator in GABA inhibition and reduced intensity of brain bioenergetic activities (Dunaev et al. 1987). In a study, chlorophyll as well as the water extract solution of *V. jatamansi* remarkably reduced ischemia and reperfusion-stimulated cerebral injury by decreasing infarct size, enhanced memory for small period, coordination with motor, lateral push response, etc. (Rehni et al. 2007).

Roots derived valepotriates and jatamanvaltrate N of *V. jatamansi* demonstrated weaker neuroprotective property (Xu et al. 2012a). Likewise, moderate neuroprotective activities of jatairidoids A, B and C were demonstrated against MPP^+-stimulated neuronal cell death in SH-SY5Y cells of human dopaminergic neuroblastoma (Xu et al. 2012b). Jatamandoid A, valeriotriate B and jatamanvaltrate G, extracted from plant demonstrated moderate nervous system protective property against MPP^+-induced neuronal SH-SY5Y cell death (Xu et al. 2012c). Study showed that valeriotriate B and jatamanvaltrate G exerted reasonable neuroprotective activity, whereas jatamandoid A displayed highest property (Xu et al. 2012c). Likewise, jatadoids A, jatamanvaltrate H, valerilactones A, valerilactones B, bakkenollides and bakkenollide-H isolated from this plant also demonstrated robust nervous system protective activities against MPP^+-stimulated neuroblastoma SH-SY5Y cells by MTT assay (Xu et al. 2011a, 2012d).

V. jatamansi rhizome extract was analyzed for antioxidants and anti-inflammation property in MPTP-sensitized rats with Parkinson's disease. Results displayed that administration of extract remarkably recovered the changed behavior test scores, TH + cell count in mid-brain, striatal dopamine levels and TH protein amount, enhanced expression of GFAP and the alterations detected in Parkinson's disease-stimulated rats using histopathology. Likewise, reduced antioxidants level and considerably enhanced ROS, LPO and inflammatory cytokine level following the supplementation is found. Valeric acid obtained from this herb comprises similar structure to the GABA of the extract, a well-known neurotransmitter and performed as an antagonist to NMDA receptor. Neuroprotective activity of valeric acid derived from Indian Valerian is determined by improvement of tracerebroventricular streptozotocin-stimulated neurodegeneration which is demonstrated in Wistar rats (Vishwakarma et al. 2016). *V. jatamansi* 100 and 200 mg/kg extract and 20 and 40 mg/kg of valeric acid considerably reduced the retention transfer latency and escape latency than the intracerebroventricular-STZ group. The extract and valeric acid of the species reduced lipid peroxidation amount and restored the amount of glutathione in mice brains. Picrotoxin supplementation considerably inverted the properties of species extract in addition to valeric acid in intracerebroventricular-STZ-administered mice. These findings indicated the considerable GABAergic activity of valeric acid in attenuation of dementia induced by experiments. Pharmacological properties of few dominant *V. jatamansi* constituents are presented in Table 5.2.

Table 5.2 Pharmacological activities of some major compounds extracted from *Valeriana jatamansi*

S. No.	Compound	Biological activity	Description	References
1	Valtrate	Cytotoxic activity	Valtrate (40 μM) in the cultures of HTC hepatoma cells cause the disappearance of membrane microvilli, a large distension of the endoplasmic reticulum and a marked condensation of the mitochondria	Keochanthala-Bounthanh et al. (1993)
		Cytotoxic effects	Exhibited property opposite to lung adenocarcinoma (A549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel7402) cell lines, with IC_{50} values ranging from 1.0 to 7.4 μM	Lin et al. (2009)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
2	Didrovaltrate	Cytotoxic activity	Didrovaltrate (80 μM) in the cultures of HTC hepatoma cells caused disappearance of membrane microvilli, a large distension of the endoplasmic reticulum and a marked condensation of the mitochondria	Keochanthala-Bounthanh et al. (1993)
3	Valerenic acid	Sedative and anxiolytic property	Reduced the breakdown of GABA in the brain and acts as $GABA_A$ receptor substrate resulting in its sedative and anxiolytic effects	Houghton (1999)
4	6-methylapigenin	Anxiolytic effects and tranquilizing properties	Supplementation of mice at intraperitoneal dose of 30 g per mouse showed anxiolytic property in rats. The bioavailability of this compound in crude infusion partially elucidates its tranquilizing effects	Wasowski et al. (2002)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
5	2S(-)-hesperidin	Sedative and sleep-enhancing properties	Exhibited reduction in ambulatory locomotor property, reduced the exploration of holes and the number of rearing in the hole-board test and enhanced the sodium thiopental-stimulated sleeping time. The depressant activity was concentration-dependent. Noteworthy moderate activity on the time spent head-dipping and on thiopental-stimulated sleeping time was observed on 2 mg/kg of hesperidin injection i.p.	Marder et al. (2003)
6	Didrovaltrate acetoxyhydrin	Cytotoxic effects	Displayed property against lung adenocarcinoma (A549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel7402) cell lines, with IC_{50} values ranging from 1.0 to 7.4 μM	Lin et al. (2009)
7	IVHD-valtrate	Cytotoxic effects	Exhibited property opposite to lung adenocarcinoma (A549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel7402) cell lines, with IC_{50} values ranging from 1.0 to 7.4 μM	Lin et al. (2009)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
8	5-hydroxydidrovaltrate	Cytotoxic effects	Demonstrated effects against lung adenocarcinoma (A549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel7402) cell lines, with IC_{50} values ranging from 1.0 to 7.4 μM	Lin et al. (2009)
9	Acevaltrate	Cytotoxic effects	Showed activity against lung adenocarcinoma (A549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel7402) cell lines, with IC_{50} values ranging from 1.0 to 7.4 μM	Lin et al. (2009)
10	Jatamanvaltrates A-M	Cytotoxic effects	Demonstrated cytotoxic effects against the PC-3 M cell line, in the IC_{50} value range of 1.4–6.3 μM except for compounds jatamanvaltrates C and jatamanvaltrates E	Lin et al. (2009)
11	Valeriotetrate A	Cytotoxic effects	Demonstrated cytotoxic activity against the PC-3 M cell line, in the IC_{50} value range of 1.4-6.3 μM	Lin et al. (2009)
12	Valeriotriate B	Cytotoxic effects	Demonstrated cytotoxicity against the PC-3 M cell line (IC_{50} value ranged from 1.4 to 6.3 μM)	Lin et al. (2009)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
13	Didrovaltrate	Cytotoxic effects	Demonstrated cytotoxicity against the PC-3 M cell line with IC_{50} value ranged from 1.4–6.3 μM	Lin et al. (2009)
14	Valeriandoids A & C	Neuroprotective effects	Displayed moderate neuroprotective effects opposite to 1-methyl-4-phenylpyridinium (MPP^+)-stimulated neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells. These compounds (3–30 μM) neither affected the cell viability nor exhibited any cytotoxic property in the absence of MPP^+	Xu et al. (2011b)
15	Chlorovaltrate	Neuroprotective effects	Displayed moderate neuroprotective effects against 1-methyl-4-phenylpyridinium (MPP^+)-stimulated neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells. These compounds (3–30 μM) neither affected the cell viability nor demonstrated any cytotoxicity with the absence of MPP^+	Xu et al. (2011b)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
	Chlorovaltrate	Cytotoxic effects	Exhibited modest cytotoxicity against lung adenocarcinoma (A 549), metastatic prostate cancer(PC-3 M), colon cancer (HCT-8) and hepatoma (Bel 7402) cell lines, with IC_{50} values of 0.89–9.76 μM	Lin et al. (2013)
16	1,5-dihydroxy-3,8-epoxyvalechlorine	Neuroprotective effects	Presented moderate neuroprotective properties against 1-methyl-4-phenylpyridinium (MPP^+)-stimulated neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells.	Xu et al. (2011b)
17	Jatamandoid A	Neuroprotective effects	Exhibited reasonable neuroprotective effects in human dopaminergic SH-SY5Y cells (CRL-2266) pretreated with several doses (3, 10 and 30 mM) of constituents before incubation in medium containing MPP^+ (0.8 mM) for stimulating neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells	Xu et al., 2012c

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
18	Valeriotriate B	Neuroprotective effects	Demonstrated moderate neuroprotective activities in human dopaminergic SH-SY5Y cells (CRL-2266) pretreated with different doses (3, 10 and v30 mM) of compounds before incubation in medium comprising MPP^+ (0.8 mM) for inducing neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells	Xu et al. (2012c)
19	Jatamanvaltrate G	Neuroprotective effects	Exhibited moderate neuroprotective effects in human dopaminergic SH-SY5Y cells (CRL-2266) pretreated with various concentrations (3, 10 and 30 mM) of compounds before incubation in medium containing MPP^+ (0.8 mM) for stimulating neuronal cell death in dopaminergic neuroblastoma SH-SY5Y cells	Xu et al. (2012c)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
20	Volvaltrate B	Cytotoxic activity	Showed cytotoxic activity against the lung adenocarcinoma (A549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel7402) cell lines, with IC_{50} values of 8.5, 2.0, 3.2 and 6.1 μM, respectively	Lin et al. (2010)
21	Valerilactones A	Neuroprotective effects	Demonstrated neuroprotective properties opposite to MPP^+-stimulated neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells, administered with several concentrations (1.5, 5 and 15 μM) of compounds before incubation in a medium containing 0.8 mM MPP^+	Xu et al. (2011a, 2012d)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
22	Valerilactones B	Neuroprotective effects	Demonstrated neuroprotective effects against MPP^+-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells treated with various concentrations (1.5, 5 and 15 μM) of compounds before incubation in a medium containing 0.8 mM MPP^+	Xu et al. (2011a, 2012d)
23	Bakkenolide-H	Neuroprotective effects	Demonstrated neuroprotective effects against MPP^+ -induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells treated with various concentrations (1.5, 5 and 15 μM) of compounds before incubation in a medium containing 0.8 mM MPP^+	Xu et al. (2011a)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
24	Jatadoids A	Neuroprotective effects	Displayed moderate neuroprotective effects against MPP^+-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells. These active compounds (3–30 μM) neither affected the cell viability nor showed any cytotoxicity in the absence of MPP^+	Xu et al. (2011a, 2012d)
25	Jatamanvaltrate H	Neuroprotective effects	Displayed moderate neuroprotective effects against MPP^+-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells. These active compounds (3–30 μM) neither affected the cell viability nor showed any cytotoxicity in the absence of MPP^+	Xu et al. (2011a, 2012d)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
26	Jatairidoids A–C	Neuroprotective effects	Displayed moderate neuroprotective effects in MPP^+-induced neuronal cell death in human dopaminergic neuroblastoma SH-SY5Y cells. The above active compounds (3–30 μm) neither affected the cell viability nor showed any cytotoxicity on SH-SY5Y cell in absence of MPP^+	Xu et al. (2012b)
27	Chlorovaltrates K-N	Cytotoxic effects	Exhibited moderate cytotoxicity against lung adenocarcinoma (A 549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel 7402) cell lines with IC_{50} values of 0.89–9.76 μM	Lin et al. (2013)
28	Rupesin B	Cytotoxic effects	Exhibited moderate cytotoxicity against lung adenocarcinoma (A 549), metastatic prostate cancer (PC-3 M), colon cancer (HCT-8) and hepatoma (Bel 7402) cell lines, with IC_{50} values of 0.89–9.76 μM	Lin et al. (2013)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
29	Valtrals A–C and Jatamanvaltrates P–Y	Cytotoxic activity	Demonstrated selective cytotoxic effects against metastatic prostate cancer (PC-3 M) and colon cancer (HCT-8) cell lines	Lin et al. (2015a, b)
30	Jatamanvaltrates R-S	Acetylcholinesterase (AChE) inhibitory activity	All these compounds exhibited acetylcholinesterase activity inhibition ratios of less than 10% at the concentration of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
31	Jatamanin Q	Acetylcholinesterase (AChE) inhibitory activity	All of the constituents showed acetylcholinesterase property prevention ratios of less than 10% at the dose of 50 μM. The positive control, tacrine, exerted an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
32	Valerianananoids D–E	Acetylcholinesterase (AChE) inhibitory activity	Studied compounds displayed acetylcholinesterase property inhibition ratios of less than 10% at the dose of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
33	Clovane-2β-isovaleroxy-9α-olvalerianananoids A-C	Acetylcholinesterase (AChE) inhibitory activity	This compound exerted acetylcholinesterase activity inhibition ratios of less than 10% at the amount of 50 μM. The positive control, tacrine, exhibited an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
34	Volvaltrate B	Acetylcholinesterase (AChE) inhibitory activity	The compound possesses acetylcholinesterase activity inhibition proportion of less than 10% at the quantity of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
35	Valeriotetrate A	Acetylcholinesterase (AChE) inhibitory activity	Exhibited acetylcholinesterase activity inhibition ratios of less than 10% at the concentration of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
36	Valeriotetrate B	Acetylcholinesterase (AChE) inhibitory activity	Displayed acetylcholinesterase activity inhibition ratios of less than 10% at the concentration of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
37	8, 11-desoidodidrovaltrate	Acetylcholinesterase (AChE) inhibitory activity	Showed acetylcholinesterase activity inhibition ratios of less than 10% at the concentration of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
38	Rupesin E	Acetylcholinesterase (AChE) inhibitory activity	Demonstrated acetylcholinesterase activity inhibition ratios of less than 10% at the concentration of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
39	(3S, 4R, 5S, 7S, 8S, 9S)-3, 8-ethoxy-7-hydroxy-4, 8-dimethylperhydrocyclopenta [c] pyran	Acetylcholinesterase (AChE) inhibitory activity	Exhibited acetylcholinesterase activity inhibition ratios of less than 10% at the concentration of 50 μM. The positive control, tacrine, showed an inhibition rate of 47.6% at 0.33 μM	Dong et al. (2015)
40	Isopatriniosine	Neuroprotective effects	Exhibited moderate neuroprotective effects against $CoCl_2$-induced neuronal cell death in PC12 cells	Tan et al. (2016)
41	Valeric acid	Neurodegeneration	Administration of Wistar Albino rats with valeric acid 20 and 40 mg/kg, i.p. (suspended in 1% Tween 80 solution) significantly decrease escape latency and retention transfer latency, then the intracerebroventricular streptozotocin group	Vishwakarma et al. (2016)

(continued)

Table 5.2 (continued)

S. No.	Compound	Biological activity	Description	References
42	Jatamanvaltrate P	Anticancer effects	Jatamanvaltrate P prevented the development and proliferation of MCF-7 and triple-negative breast cancer (TNBC) cell lines (MDA-MB-231, MDA-MB-453 and MDA-MB-468) in a concentration-based fashion. Also whereas displayed moderately low cytotoxic effects to human breast epithelial cells (MCF-10A). Administration with jatamanvaltrate P stimulated G2/M phase arrest in TNBC and G0/G1-phase arrest in MCF-7 cells	Yang et al. (2017)
43	Jatamanvaltrates N	Neuroprotective activity	Exhibited weak neuroprotective property	Xu et al. (2012a)
44	(+)-9′-Isovaleroxylariciresinol	Cytotoxicity	Significant in vitro cytotoxicity was revealed against PC-3 M and HCT-8 cell lines with IC_{50} values of 8.1 and 5.3 μM respectively	Lin et al. (2010)

5.4.2.1 Sedative and Tranquillizing Effect

Various sleeping disorders in human are effectively treated with *V. jatamansi*. Tranquilizing property is exhibited by valerenic acids (like monoterpenes and sesquiterpenes) and glycosides of iridoid from the species. Clinical studies on Tagar have established that the species root extract reduced sleep latency, improve the quality of sleep and, therefore, observed to be beneficial in administration of nervousness and sleeplessness (Leathwood and Chauffard 1983). Valerenal and few other constituents extracted from *V. jatamansi* exerted sedative property to the valepotriates fractions and essential oil (Wagner et al. 1980; Hendricks et al. 1981). Studies demonstrated that decomposition by products of valepotriates like baldrinal, homobaldrinal, decylbaldrinal and valtroxal reduced sedative activity to some extent and property also caused considerable mortality in mice (Schneider and Willems 1982). It is reported that valerenic acid prevents the enzyme system association with central GABA catabolism (Riedel et al. 1982) and is released by [3H] GABA valerian extract through reverse of GABA transporter, which depends on Na^+ and independent on Ca^{++} (Santos et al. 1994). The enhancement in [3H] GABA discharge was not found dependent on Na^+-K^+-ATPase property and the membrane potential. Root extract of *V. jatamansi* used for commercial purpose displayed pronounced sedative activities in the rats in relation to a reduced motility and an enhanced thiopental sleeping time (Leuschner et al. 1993). Comparative analysis of *V. jatamansi* extract with chlorpromazine and diazepam exhibited moderate sedative property (Leuschner et al. 1993). Sedative property was also potentiated by flavanone glycoside 2S (-) hesperidin extracted from this herb (Marder et al. 2003). Sedative property of hesperidin and 6- methylapigenin is also validated by in vivo experiments using mice as an experimental model (Marder et al. 2003). Anticonvulsant and soothing properties are exerted by glycosides of flavonoid, namely linarin and hesperidin which probably interacted with GABAA receptors (Fernandez et al. 2004). Sleep–wake profile and EEG delta property in male Sprague-Dawley rats administered with different quantities ranged from 100 to 300 mg/kg of this plant were determined. The results exhibited that non-rapid eye movement sleep delta activity (sustained for 8 h) and sleep latency were considerable after extract supplementation at 300 mg/kg dose. The duration of wake state at 200 and 300 mg dose was significantly increased. Study exhibited that extract of the roots remarkably reduced sleep latency, NREM sleep, increased duration of total sleep and reduced wakefulness period in administered animals. Hence, root extract of *V. jatamansi* attenuates the quality of sleep and control monoamine amount in mice brain (Sahu et al. 2012).

5.4.2.2 Anxiolytic Property

4′, 5, 7-dihydroxy-6-methylflavone or 6-methylapigenin (MA) extracted from *V. jatamansi* exerted anxiolytic activity (Wasowski et al. 2002). Anxiolytic effect of valtrate extracted from this herb is investigated in mice by supplementing with varying doses of valtrate for 10 days after successive disclosure to open field test (OFT) and elevated

plus-maze (EPM) test (Shi et al. 2014). Valtrate displayed the anxiolytic property in mice by enhancing open arm entry percentage and time in the EPM assay and central entries number in the OFT. Further, remarkable decrease in amount of corticosterone in rat serum was recorded. The findings from the study indicated that valtrate exerts anxiolytic property of behavioral models which may be mediated by hypothalamus–pituitary–adrenal axis function (Shi et al. 2014).

Gene expression of apoptosis-related genes was measured in the control and administered groups of mice anxiety model using Gene chip technology. Differences in expression of gene related to apoptosis in standard mice, anxiety model mice and mice administered with *V. jatamansi* extract were recorded. Ets-1, Elk-1, Bax, Apaf-1 and Bcl-2 gene expression in the model group were up-regulated than the normal group, but in other groups the gene was expressed. Finding showed this plant plays important part to control the irregular expression of genes associated with apoptosis in rat model animal (Yan et al. 2011).

5.4.2.3 Antidepressant Activity

Tager extract is used to reduce anxiety, stress and ameliorate depression symptoms (Bhattacharya et al. 2007). The species extract considerably decreased locomotor action at 200 mg/Kg dose using tail suspension method and comprises an adverse interplay with antidepressant-like activity. Methanolic and ethanol aqueous extracts of the plant exhibited that such activity of the species is not dependent on the level of terpenoids present (Subhan et al. 2010). However, a remarkable amount of antilocomotor property was detected at the high terpenoids amount using tail swim assay or forced swim assessment (Subhan et al. 2010). Extract of patchouli alcohol chemotype of *V. jatamansi* is also displayed as antidepressant property in the extract in dichloromethane of patchouli alcohol chemotype of *V. jatamansi* (Sah et al. 2011). Rhizomes and roots of the herb were gathered, dried, extracted using dichloromethane and utilized for evaluation of antidepressant property in albino LACA rats by forced swim method. Results suggested that single dose (40 mg/kg extract) supplementation considerably prevented the immobility time in rats. In chronic study, remarkable decline in the immobility period and enhanced amount of norepinephrine and dopamine in mice forebrain was found to indicate the antidepressant property of this species.

5.4.2.4 Antispasmolytic and Blood Pressure Decreasing Activity

Crude rhizome extract derived from *V. jatamansi* and its fractions showed antspasmolytic and blood pressure decreasing property (Gilani et al. 2005). Crude extract (0.1–3.0 mg/mL) when tested against high K^+ (80 mM)-stimulated contractions in rabbit jejunum preparations, generated low preventive action but totally relax the shrinkages stimulated by small K^+ (20 mM). Plant extract produced same results in ileum of guinea pig as in jejunum of rabbit. The study also demonstrated the blood

pressure reducing property of the *V. jatamansi* in mice by intravenous supplementation of extract (10–100 mg/kg). A concentration-based decrease in average arterial blood pressure was observed in normotensive mice treated with anesthesia. Findings from the report exhibited hypertensive property of valeranone which is responsible for blood pressure reducing activity of the species (Arora and Arora 1963). Likewise, Wagner et al. (1980) reported the spasmolytic activity of iridoids valtrate and didrovaltrate of *V. jatamansi*. The marketable combination of iridoids was detected to be active than the papaverine in similar amount (Gilani et al. 2005). Blood pressure reducing and antispasmodic property of *V. jatamansi* roots displayed the facilitation of these properties by K^+ (ATP) channel activation hence warranted the utility of this herb in gastrointestinal and cardiovascular complaints (Gilani et al. 2005).

5.4.2.5 Gastrointestinal and Cardiovascular Ailment

Diverse gastrointestinal complaints like diarrhea, stomach cramp, diverticulitis, irritable bowl, dyspepsia related to nervous system, stomach cramp and stimulates digestion are treated using *V. jatamansi* (Houghton 1999). Species extract is observed to decrease blood pressure and strengthening and heart palpitations (Morazzoni and Bombardelli 1995). Antispasmodic and hypotensive property of this herbal plant was demonstrated to be probably intervened through KATP channel initiation and provide evidences on utilization of species in these diseases (Gilani et al. 2005). Irritable bowel syndrome treatment using iridoids from *V. jatamansi* was also analyzed in male Sprague-Dawley mice. The model was established by chronic stress and independent feeding. The amount of colon 5-HT content is enhanced considerably in model group, but it reduced remarkably in hypothalamic region. The three groups administered with iridoid exhibits reduced 5-HT amount in serum and colon; nevertheless, the amount of 5-HT in hypothalamic region enhanced while no remarkable alterations are screened in 5-HIAA. However, colon and serum 5-HT/5-HIAA amount are decreased. The action mechanism of iridoids in irritable bowel syndrome can be associated with controlling the influence level by gastrointestinal 5-HT to CNS (Yan et al. 2011).

5.4.2.6 Antidiarrheal and Bronchodilatory Potential

V. jatamansi is found to possess antidiarrheal and bronchodilatory effects using in vivo method (Khan and Gilani 2011). Defensive property of *V. jatamansi* crude extract was screened against castor oil-stimulated diarrhea in rats. Pre-administration of crude extract to mice developed 20% and 60% defense against diarrhea at 300 mg/kg and 600 mg/kg doses, respectively, then the control. Hence, findings exhibited that *V. jatamansi* extract prevented the diarrhea stimulated by castor oil.

5.4.2.7 Anti-inflammatory Activity

Crude *V. jatamansi* leaves extract demonstrated anti-inflammation by in vitro and in vivo assays (Khuda et al. 2013). Dried leaves were powdered, and methanol extracted material of the species was filtered and concentrated to obtain crude extract. The obtained material was dissolved in dH_2O and partitioned to obtain chloroform, n-butanol, ethyl acetate, n-hexane and aqueous fractions. The methanolic extract topical formulation (cream) was tested in male Wistar rats using carrageen stimulated hind paw edema assay and its impact on inflammation models in acute and chronic stage. All the fractions with methanolic extract screened for anti-inflammation property by in vitro lipoxygenase prevention method. The species extract displayed considerable anti-inflammatory property then the standard (10%) followed by 5 h of carrageen injection. This anti-inflammatory property was also detected in ethyl acetate fraction during in vitro testing ($IC_{50} = 76 \pm 0.14$) then the standard ($IC_{50} = 6.11 \pm 0.02$). Study exhibited that the fraction of ethyl acetate may be utilized for the extraction of novel principal compound with anti-inflammatory property. Methanol and ethanol prepared extract of *V. jatamansi* also comprises anti-inflammatory effects (Subhan et al. 2007) and found to prevent mediators generated during inflammation like prostaglandins, serotonin, histamine and bradykinins (Vinegar et al. 1969). Other studies also displayed the anti-inflammatory effects of crude extract and volatile oils of *V. jatamansi* (Subhan et al. 2007; Agnihotri et al. 2011).

5.4.2.8 Analgesic Properties

Dried material (rhizomes and roots) was extracted in dichloromethane and essential oil. LACA mice (20–40 g) were supplemented with acetic acid (1%) by intraperitoneal injection. The writhing reaction was characterized by abdominal contraction and hind limb stretching counted for 10 min (Sah et al. 2010b). Extract doses, oil and aspirin were used to treat rats for 1 h prior to assessment through oral mode. It is observed that dichloromethane extract and oil considerably prevented the number of writhing than the control group. However, extract and essential oil did not exhibit any property in tail flick model which showed only peripheral analgesic property. Further, the action mechanism of acetic acid stimulated writhing exhibited that subeffective volatile oil dosage remarkably enhances activity of aspirin, whereas such effects were not recorded in the case of extract. It was found that essential oil displayed peripheral analgesic property via inhibition synthesis of prostaglandins.

5.4.2.9 Cytotoxic Activity

Cytotoxicity of several constituents isolated from this species demonstrated different level of counteracting activities on the cancer cells growth and proliferation.

Numerous valepotriates displayed cytotoxic and antitumor properties. Jatamanvalterate, an iridoids ester extracted from the species, exerted notable antitumor activities (Yang et al. 2017). Studies (in vivo and in vitro) exhibited growth inhibition and proliferation of breast cancer (TNBC) cell lines on concentration-based fashion but displayed lower cytotoxic property to human breast epithelial cells (MCF-10A). Jatamanvaltrate P showed a potent antitumor activity in MDA-MB-231 xenografts (Yang et al. 2017). Valtrals A, B and C three decomposition products of valepotriates possessed selective cytotoxic activity opposite to PC-3M and HCT-8 (metastatic prostate cancer cell lines and colon cancer) respectively (Lin et al. 2015b). Lin et al. (2009) studied that valtrate, acevaltrate, IVHD-valtrate, didrovaltrate acetoxy hydrin and 5-hydroxydidrovaltrate derived from the species demonstrated effects against diverse cancerous cell lines. However, acevaltrate was found the most effective compound. And all compounds except jatamanvalterate C, jatamanvaltrate E and 10-acetoxyvaltrathydrin, revealed cytotoxic property against the PC-3M cell line. In vitro and in vivo method were performed to determine anticancer property of IVHD-valtrate one among highly active constituents of *V. jatamansi*, against human ovarian cancer cells (Lin et al. 2013). IVHD-valtrate prevents the development and propagation of the A2780 and OVCAR-3 cancerous cell lines in a dose-based fashion. However, comparatively lower cytotoxicity was detected into immortalize IOSE-144 (non-tumorigenic human ovarian surface epithelial cells). IVHD-valtrate administration stimulates and arrests the OVCAR-3 cells in the G2/M phase. Preclinical results on IVHD-valtrate specified its potent as a therapeutic molecule to treat ovarian cancer along with providing strong proofs for creating novel chemotherapeutic molecule (Li et al. 2013). Likewise, cytotoxicity of 10 new compounds [jatamanvaltrates P-Y (jatamanvaltrates P R, S, T-Y along with one known valepotriate (nardostachin) extracted from *V. jatamansi* demonstrated that merely nardostachin, jatamanvaltrate P and jatamanvaltrate X exhibited stronger cytotoxic property in PC-3 cells. Lignan compound (+)-9′-isovaleroxylariciresinol was screened for cytotoxic property beside four cancerous cell lines of human namely, HCT-8, PC-3M, A54 and Bel7402 demonstrated cytotoxicity against PC-3 M and HCT-8 cell lines (Lin et al. 2010). Three newly identified minor valepotriate isomers, namely jatamanvaltrates Z1, Z2 and Z3 isolated from this plant exhibited modest cytotoxic property in cancerous cell lines A549, PC-3 M, HCT-8 and Bel7402 (lung adenocarcinoma, metastatic prostate cancer, colon cancer and hepatoma cell lines), respectively (Lin et al. 2017). Hydroethanolic extract of rhizomes of Tagar was measured in Swiss albino rats (Joseph et al. 2016). Acute toxicity analysis did not exhibit any sign of irregularity, illness or death throughout the time of analysis while administered and untreated animals displayed considerable variations in auditory startle loss, fierceness (untreated > administered), nasal discharge and dyspnoea. Additionally, photoactometer test demonstrated dose-based enhancement in sedative quality. The findings revealed that hydroethanolic extract didn't exhibit any morbidity, mortality, or any other negative impact on healthy Swiss albino rat neither in single oral dose nor in chronic doses on administration.

5.4.2.10 Constipation and Antinociceptive Effect

Shade dried fresh leaves of *V. jatamansi* was coarsely powdered and soaked in 70% ethanol. Extract was obtained by filtering the solution and evaporating the filtrate followed by solubilizing in distilled water. The extract of the species caused dose-based (3–10 mg/mL) contractile activity in separated ileum of guinea pig. It was found that pre-administration of tissues with atropine (1 μM) remove the stimulatory activity of crude extract. These finding exhibited that the spasmogenic property of *V. jatamansi* is mediated possibly by the activation of muscarinic receptors, which provides strong evidences for the use of *V. jatamansi* in constipation (Khan and Gilani 2011).

V. jatamansi extract was determined for antinociceptive effect by using stimulated writhing and tail flick model (Sah et al. 2010b). Intraperitoneal injection of acetic acid to Lacamice develops writhing response depicted through constriction in abdomen and stretches in hind limb. Varying extract and volatile oil doses p.o. were supplemented 1 h prior to injecting acetic acid. Acetic acid stimulated writhing was inhibited significantly by both the extract and essential oil and enhanced the latency time after 2 h of treatment in tail flick model. Essential oil in subeffective doses considerably potentiated the effects of aspirin while no such property was detected in extract. Likewise, in tail flick test the analgesic effects of essential oil were completely antagonized by naloxone while no such effects were observed using extracts. These findings showed that both poor central and a strong peripheral antinociceptive property of the maaliol-type *V. jatamansi* chemotype.

5.4.2.11 Cure Liver Cirrhosis and Tissue Hyperproliferative Response

Rhizome extract of *V. jatamansi* was tested on the liver cirrhosis animal model rats and on cell proliferation (Prasad et al. 2010). Liver cirrhosis was stimulated in rats treated with thioacetamide (0.03%). Rats were then administrated with the extract orally for 9 weeks. Results elucidated that the extract of *V. jatamansi* partially revert the enhanced amount of alkaline phosphatase, γ-glutamyl transferase and choose biochemical markers related to hepatic injury along with the drug-metabolizing enzymes. Histopathological analysis of hepatic tissue validated the therapeutic potential of species authenticated through alterations in biochemicals.

5.4.2.12 Anti-HCV Property

The water, chloroform and methanol pulverized root samples of *V. jatamansi* were extracted and screened for anti-Hepatitis C virus (HCV) property (Ganta et al. 2017). Based on primary bioassay testing, the methanolic extract was identified and applied for fractionation through preparative TLC. Fractions (4 nos.) F1–F4 were gathered from the TLC plate, isolated separately with ethyl acetate and freeze-dried. Overnight grown cells of human hepatoma cell line (Huh-7.5 cells) were infested with viral

supernatant (J6/JFH chimeric HCV strain). PBS is used to wash cells and varying extracts doses or corresponding volume of DMSO was added as control. Antiviral activity was demonstrated by RT-PCR and western blotting. Result displayed that metabolic extract showed decline in HCV replication and F4 fraction exhibited remarkable viral prevention. Additionally, sharp quenching of inherent fluorescence with enhanced extract concentration was observed in the presence of fraction F4 using intrinsic fluorescence assay of purified HCV RNA-dependent RNA polymerase NS5B. These findings revealed that methanol extract of *V. jatamansi* and F4 fraction prevented HCV through interaction with HCV NS5B protein (Ganta et al. 2017).

5.4.2.13 Regulation of Lipid Metabolism

IRFV (Iridoids rich fraction of *V. jatamansi*) was investigated to measure the control of lipid metabolism and mechanism linked with it (Zhu et al. 2016). Hyperlipidemic mice were fed with different amount of IRFV. The findings displayed that three varying dosages of iridoid-rich fraction decreases the body weight, durenes (assurance) triglyceride amount and enhance serum high density lipoprotein cholesterol content in the supplemented animals with fraction. Low iridoid-rich dosage remarkably reduces the aspartate aminotransferase and alanine aminotransferase in serum, liver index and liver triglyceride level but increased the property of lipoprotein lipase. Medium IRFV dosage can considerably decline the LDL-C and TG level in liver. However, high iridoid dosage remarkably declines the serum LDL-C, AST, TBA and ALT level and enhanced HL activity. Considerable incline in expression of PPAR-d and ApoA5 and decline in the protein SREBP-1c expression was detected by three varying iridoid dosages. Pathological investigation of liver tissue showed that iridoid can ameliorate cell deterioration to a certain extent. The findings from this study showed that iridoid-rich fraction plays essential roles in metabolism of lipid and its mechanism might be associated with enhanced expression of ApoA5 protein.

5.4.2.14 Adaptogenic Activity

V. jatamansi extract was evaluated for adaptogenic property in inbred male Sprague–Dawley rats (Sharma et al. 2012a). Rats were kept inside the cages made up of polypropylene under a regulated environment. The results exhibited that *V. jatamansi* extract at single oral dose (200 mg/kg) displayed highest adaptiveness in cold-hypoxia-restraint rats. Moreover, supplementation of the highest effective quantity of 200 mg/kg (single dose/day, for 5 days) was unable to provide additional adaptogenic property. These finding revealed that species extract do not exhibit cumulative adaptogenic property.

5.4.2.15 Enzyme Inhibition Activity

Acetylcholinesterase, butyrylcholinesterase and α-glucosidase enzyme-preventing properties of unrefined *V. jatamansi* infusion and its subsequent fractions were performed (Khuda et al. 2014). It was observed that crude extract comprises considerable property against cholinesterases. Likewise, chloroform fractions of *V. jatamansi* showed remarkable property against enzyme acetylcholinesterase (IC_{50}: 61 μg/ml) while ethyl acetate fractions exhibits considerable property against enzymes butyrylcholinesterase (IC_{50}: 58 μg/ml). Findings from the study showed enormous therapeutic potential of *V. jatamansi* for discovery of novel active constituents for treating mental abnormality for example Alzheimer's disease.

5.4.2.16 Antioxidant and Antimicrobial Properties

Various reports are available on antioxidant properties of *V. jatamansi*. For example, Kalim et al. (2010) studied the species root extracts for antioxidant activity. Hydroxyl radical, peroxynitrite scavenging assay, non-enzymatic superoxide radical scavenging assay and nitric oxide scavenging property method exhibited high antioxidant activity. Antioxidant property of methanol extracts and essential oil derived from species roots was analyzed (Thusoo et al. 2014). *V. jatamansi* essential oil and supercritical CO_2 fluid extracts was measured for antioxidant activity using DPPH radical, superoxide radical and hydroxyl scavenging assays (Pandian and Nagarajan 2015). Bhatt et al. (2012) measured the antioxidant property of root sample obtained from planted and wild source using DPPH and FRAP assay. Likewise, antioxidant property of essential oil was measured by DPPH assay. Comparative assessment of planted root samples and wild genotypes demonstrated considerably maximum antioxidant activity (ABTS–4.87 mg/g: FRAP–10.18 mg/g AAE d.w.). While antioxidant property measured by DPPH activity was more in wild source. Essential oil displayed strong antioxidant activity than the methanolic extract. Moreover, several biochemical and ISSR (inter simple sequence repeats) markers were detected to linked with the antioxidant property and valerenic acid content of *V. jatamansi* determined by ABTS, DPPH and FRAP assay and their possible uses in selection of material with quality traits for breeding was visualized (Jugran et al. 2013b, 2015b). ABTS, DPPH and FRAP assays were conducted to measure antioxidants in aerial and root parts extract of 25 distant populations of *V. jatamansi* collected from Uttarakhand (Jugran et al. 2016a). Considerable variations in antioxidant property across the population were recorded. Results indicated that *V. jatamansi* can be considered as a natural source of antioxidant. However, no clear trend was detected in antioxidants activity across the altitudinal range in this study, but among diverse habitats (oak, pine, mixed forest type and grassy land) differences in antioxidant property were recorded. The effect of arbuscular mycorrhizal fungi (AMF) on antioxidant property in aerial and root parts investigated using DPPH, FRAP and ABTS assay demonstrated considerable variations among plants of 1st and 2nd years of plantation. The

results demonstrated that inoculation with AMF increased antioxidant activity which suggests a positive effect of AMF inoculation on species (Jugran et al. 2015d).

V. jatamansi reported to possess antibacterial and antifungal property against enormous number of bacterial and fungal pathogens (Suri and Thind 1978; Thind and Suri 1979; Girgune et al. 1980). *V. jatamansi* extract in various solvent system (methanol, chloroform, hexane and water) showed higher antimicrobial property than the standard—Ampicillin and Erythromycin (Sati et al. 2011). Extract of *V. jatamansi* aerial part was investigated for antimicrobial property. The chloroform fraction of the species exhibited considerable property over *Staphylococcus aureus* while hexane fraction displayed maximum property opposite to *Bacillus subtilus* (Khuda et al. 2012). However, hexane fraction of the herb demonstrated potent preventive activity against *Microsporum canis* while chloroform and water fraction counter the activity of *M. canis* and *Aspergillus flavus.* Essential oil derived from extract of *V. jatamansi* whole plant was studied for the potential antimicrobial property against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus pumilus* and *Candida albicans* (Agnihotri et al. 2011). In another study, hydro-alcohol (50% v/v) and hexane extract of *V. jatamansi* were tested for antimicrobial property against pathogenic and drug-resistant strains. Potent antimicrobial property was demonstrated by hydro-alcoholic extract counter *Micrococcus luteus*, *Escherichia coli*, *Escherichia coli mutans*, *Salmonella abony*, *Lactobacillus plantarum* and *Staphylococcus epidermidis.* Both the extracts displayed potent sensitivity against multi-drug-resistant *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Moreover, only hydroalcoholic extract of this plant showed good antifungal property against *Aspergillus niger* but no such property was detected against *Candida albicans* (Babu et al. 2015). Five solvent system like, water, methanol, ethanol, acetone and hexane was used for root material extraction of *V. jatamansi* to analyze the antimicrobial property. Species extract in ethanol exhibited highest property opposite to all studied bacterial strains excluding *Bacillus subtilis* that displayed sensitivity to acetone extract. Further, extracts in all type of solvents prevent the development of *Escherichia coli.* However, hexane extract of species demonstrated antifungal activity against *Aspergillus flavus*, *Aspergillus fumigatus* and *Candida albicans* whereas *Aspergillus fumigatus* exhibited sensitivity at high dose against hexane extract. Moreover, bacterial strain showed much sensitivity to the *V. jatamansi* methanol extract (Rawat et al. 2017).

5.4.2.17 Other Uses

V. jatamansi is used either alone or in combination for the preparation of several herbal formulations. The plant is used for preparation of antiwrinkle cream (Ravichandran et al. 2005), and Sumenta as an antidepressant formulation (Prakash 1999). Didrovaltrate an iridoid found in *V. jatamansi* is observed to prevent alternative synthesis in the serum complement system and its likely usage in few autoimmune illnesses (Houghton 1999; Baibado and Cheung 2011). Hesperidin is a flavonoid constituents extracted from *V. jatamansi* roots was analyzed for radioprotective activity against

γ irradiation induced severe DNA injury. Hesperidin (16.38 μM dose) was found highly active in decreasing radioactivity (Katoch et al. 2012). The impact of total flavonoids isolated from these species was analyzed on TGF-beta signaling pathway in hepatocarcinoma 22-bearing rats. Four groups of hepatocarcinoma 22-bearing rats like model group, tegafur group, low and high-dose *V. jatamansi* group were divided randomly. These groups were analyzed for differences in gene expression chart of signaling pathway of TGF-beta by gene chip technology. Findings from the study exhibit expression of 7 genes were considerably controlled in other three groups than the control group in TGF-beta signaling pathway. Of which, E2f5, Cul1, Smad7 and Myc genes expression was up-regulated, while there is down-regulation in the expression of Smad1, Comp and Thbs4 genes. Total flavonoids from the herb control the unusual expression of genes involved in hepatocarcinoma 22-bearing rats with TGF-beta signaling pathway (Zhang et al. 2012).

5.5 Agrotechnology for Cultivation

IHR is a global biodiversity hotspot encompasses enormous diversity of native, endemic, rare and endangered medicinal plants. These medicinal plants appreciated across worldwide because of the presence of unique secondary metabolites for therapeutic purposes. As *V. jatamansi* is generally gathered from its natural sites to meet out the industrial demand which has severally over exploited the species and put this plant under endangered category (NMPB 2008). Therefore, there is an urgent need to attempt for its cultivation and conservation. However, only a few studies have been attempted to adopt the cultivation of these plants. Cultivation of MAPs is beneficial to develop standard agrotechniques (Fig. 5.2). It provides chances for crop variation along with income generation to the farmers. However, development of suitable cultivation packages for any medicinal plants which is collected from natural site is challenging to promote cultivation (NMPB 2008; Phondani et al. 2016; Dhiman et al. 2020). The cultivation of the *V. jatamansi* can be understood by studying the ecology and adaption situation of this species as mentioned below.

5.5.1 Climatic Conditions

V. jatamansi is a temperate herbaceous species grows well in cold winters and mild summers. This is a shade loving species observed to grow in the temperature ranging from 15 to 25 °C and with the requirement of 80–90% relative humidity (Mukherjee 2015). Seed germination of this plant is supported by high temperature at the time of sowing (Mukherjee and Chakraborty 2014). Flowerings in *V. jatamansi* started in February month and ended till April and ripening of seeds takes place in May onward (Mukherjee and Chakraborty 2014; Jugran et al. 2019). The composition of volatile constituents was investigated under the influence of genotype and environmental

Fig. 5.2 Cultivation practices of *V. jatamansi:* A&B, wild and cultivated *V. jatamansi* plants; C & D, *V. jatamansi* plants in flowering; E&F, cultivation of *V. jatamansi* at Shri Narayan Ashram, Pithoragarh, Uttarakhand, India, by GBPNIHE

variables. Various Chinese genotypes and chemotypes of Tagar collected from seven wild areas in China and common-garden specimens were recorded based on SNP and volatile constituents. Two diverse populations were differentiated from five others based on genotypes and essential oil constituents. The uniformity of samples showed that genotype could considerably affect chemotype. Volatile profiles of wild populations were different from common-garden samples which showed that chemotypes are strongly affected by environmental variables (He et al. 2018).

5.5.2 Soil Condition

Fertile, loamy soil rich in humus along with relatively slight acidic to neutral pH (6–7) condition is preferred by *V. jatamansi*. The plant can grow over an extensive range of soils, with slopes up to 20%, if adequate water and nitrogen nutrient is there (NMPB 2008). However, shallow roots of the herb are responsible for preferential moist situation and needed proper drainage as the crop plant is unable to withstand and survive with water logging condition. Harvesting of roots can be done efficiently and easily in a relatively loose soil with low clay content. Maximum development of *V. jatamansi* plants can occur in a slope of 5–6%. In humus-rich soil under shade, strong development of species is recorded than the barren rock soil on sunny spots. The shallow roots present in herb may be responsible for this due to controlling the uptake of deep soil groundwater. This can be resulted into the adaptation of *V. jatamansi* to grow under the shelter of a tree in a forest in which moisture level is high, that decreases water requirement and allow the establishment of humus from the trees dead leaves.

5.5.3 Planting Material

V. jatamansi can be cultivated through seeds and rootstocks during the post-monsoon season. However, multiplication by rhizomatous suckers is regarded as finest due to early maturation of this plant than the plants propagated through seeds. Moreover, modern biotechnological approaches like tissue culture can be an efficient method for propagation of *V. jatamansi*.

5.5.4 Methods of Propagation

Several reports are available on propagation of *V. jatamansi* using modern biotechnological techniques. Propagation of the species was carried out through seed, rhizomes and tissue culture. The propagules are multiplied at varying periods for example, April–May month are appropriate for seed sowing while plantation of rhizomes takes place in June month. The in vitro raised plantlets are also generated using explants and PGRs in several studies (Mathur et al. 1988; Purohit et al. 2015; Dhiman et al. 2020). The plantlets were than hardened out followed by field transfer.

5.5.5 Seed Germination

V. jatamansi seeds are very small and light weighted. Approximately 0.5–1.0 kg seeds are required for sowing of the species seeds per hectare area (NMPB 2008; Dhiman et al. 2020).

The species is propagated by seeds which are sown during March–April. Sowing is done in raised beds under partial shade conditions (75% shade). Due to very small size of the seeds, sowing of seeds on surface of the nursery beds followed by covering with thin layer of soil mixture is recommended. There is the requirement of light irrigation during the seed germination to keep the soil beds moist. Once seedlings reached to 2–3 leaf stage, they can be transferred in polysleeves to remove overcrowding. The transplantation of seedlings is generally done after 3–4 months (Pal et al. 2020). Mature shade dried seeds were gathered and surface sterilized with water and than sown in bed on 25th April each year under careful investigation with sterilized clay soil. The seeds were germinated at 1290, 1550, 1800 and 2000 m asl altitude in Darjeeling, India. Maximum survival percent of *V. jatamansi* plants across 1290 to 2000 m asl displayed its adaptation at a broader altitudinal range. However, findings from this study revealed low seed germination (%) above 1800 m which prohibited its cultivation potential at lower altitudinal regions only. Study demonstrated highest seed germination when seed dipped with cow urine and also exhibited parity with the pre chilled seed treatment. It was observed that seed soaked through cow urine increases 50.3% further sprouting percentage over the normal seed sown. These findings demonstrated the baseline dataset on detection of favorable cultivation sites for developing agrotechniques for conservation of genomic resources and management approaches for this plant (Mukherjee and Chakraborty 2014). The effects of varying doses of growth hormones were evaluated on seed development parameters and seedlings vitality of *V. jatamansi*. The seeds were osmo-primed with different hormone doses of IBA, GA_3 kinetin and hydroprimed with distilled water. Maximum seed sprouting percentage was recorded with 200 ppm of kinetin-treated seeds of *V. jatamansi*.

Additionally, shortest time period in days for germination of seeds was found with 250 ppm kinetin to complete 23.33 days and displayed consistency in with 200 ppm kinetin-pretreated seeds (24.33 days). Mean germination time (33.03 days) of untreated (control) seeds of the species was considerably decreased (22.95 days) when seeds soaked with GA3 250 ppm. This time was 31.88% lesser as compared to control and was at par with 23.33 days in 200 ppm kinetin-pretreated seeds. Kinetin 200 ppm pretreated seeds exhibited highest fresh weight. Similarly, considerable variation in dry weight of 2-month-old seedling phase and significantly high dry biomass was recorded with seeds pretreated with kinetin 200 ppm. The data related to the consequence of seed vigor treatments on seedling vigor index-I in species demonstrated that control seeds exhibited minimum SV-I (51.87), that was significantly low than the rest of the treatments. Seeds pretreated with 100 ppm kinetin displayed highest SV-I (303.33). Moreover, analysis demonstrated that 50 ppm kinetin exerted lowest SV-II which was same with 250 ppm IBA and control seeds recorded. The

highest SV-II (190.06) was detected in recorded 200 ppm kinetin-pretreated seeds, which was 362.32% higher as compared to control and was significantly improved to other treatments. Maximum seedling length (3.11 cm) was recorded with 200 ppm of kinetin. Highest EI was found with 200 ppm of kinetin and displayed parity with 250 ppm kinetin-pretreated seeds (Mukherjee 2018).

5.5.6 Macropropagation

Root suckers of *V. jatamansi* which can be used as a planting material is needed to maintain in a separate mother nursery. Plantation of the sucker can be done by taking out the fresh root suckers from the mother nursery for field plantation. However, the month of June or onset of monsoon is appropriate for plantation of new sucker in the nursery. The crop of *V. jatamansi* can be raised through seeds by preparing a separate nursery in April–May. The seeds are germinated within 15–20 days and placed into polybags for further development and will be ready for planting in next three month. Planting of rhizomes in June month is most favorable. However, successful multiplication can be obtained using old rhizomes/rootstock (NMPB 2008). A simple cost-effective method has been established for vegetative production of *V. jatamansi* through macroproliferation in large amounts. This method ensures that each propagule possesses some part of shoot along with rhizome part and some roots at the time of separation, ensuring rapid establishment and practically 100 per cent survival of the propagated material. The most vital component identified for the success of this method is time of separation, portion of shoot/root/rhizome to be retained in each propagule and providing suitable growing conditions for planting the propagules. The technique has been successfully applied for the production of 2.8 lakhs nursery stock of *V. jatamansi* during 2004–2008 under National Medicinal Plants Board (NMPB) funded project completed by Himalayan Forest Research Institute. A desirable number of nursery stocks were maintained permanently in the nursery for propagation in future using this technique without depleting natural population (Sharma et al. 2012b). Propagation of *V. jatamansi* plant raised by cutting and separating the rhizomes is reported to generate various plants. These plants were sown in the month of rainy season in the well-prepared field in the month of June–July (Mukherjee 2015). It is observed that spacing between plants of this herb plays considerable role in growth of fresh aerial biomass. Findings from study revealed that spacing of 30 × 45 cm at 6-, 9-, 12-, 15- and 18-month-old plants of *V. jatamansi* possess higher biomass. Transplanting time and space was well at 9-month-old stage for rhizome weight per plant than other stages to obtain underground biomass. Likewise, higher biomass of underground part was recorded in June transplanting. Space of 30 cm × 45 cm provides considerable positive response at 9- and 12-month stages of *V. jatamansi* (Mukherjee and Chakraborty 2014; Mukherjee 2015). In a study, high-altitude germplasm of *V. jatamansi* demonstrated the presence of three sex forms, namely gynoecious, gynomonoecious and bisexual. All the sex forms displayed considerable differences among all traits studied. Bisexual form exhibited

higher (16.36 g, 13.43 g) dry aerial biomass and dry rootstock biomass under open condition followed by gynomonoecious and gynoecious forms, respectively. Hence, plantation of the bisexual form of the species in open environment is suggested for high biomass yield and for commercial cultivation (Karnwal et al. 2012).

5.5.7 Biotechnological Intervention

5.5.7.1 Micropropagation

Several studies have been attempted for faster clonal and large quantity generation of MAPs with threatened endangered and rare status using modern biotechnological tools (Abraham et al. 2010). Various protocols have been established by using different types of explants of this species (Table 5.3). Adventitious shoots and somatic embryos from embryogenic callus were induced from in vitro raised *V. jatamansi* leaves. Both morphogenic developments could be stimulated on MS basal medium supplemented with varying concentrations and combinations of PGRs. Embryogenic callus, stimulated solely in the presence of 1.0–7.5 μM 2,4-D and 5.0 μM α- NAA, differentiated into adventitious shoots and somatic embryos, respectively when left on the same medium. Callus on MS medium having IBA (5.0 μM), NAA (5.0 μM) or 2,4-D (1–5 μM) stimulated the development of adventitious roots. Cytokinins that were added singly to callus initiation medium, containing 6-BA, kinetin and thidiazuron, were unable to stimulate callus at 5.0 μM except when pooled with 0.25–1.0 μM NAA (Chen et al. 2014). Purohit et al. (2015) reported the effective in vitro regeneration protocol for this herb using Nodal explants in MS basal medium containing with PGRs. Different combinations of 1.5 μM BAP, 0.5 μM NAA and 0.1 μM GA_3 in the medium exhibited maximum mean shoot length, shoot number and leaf number. A hundred percent rooting with significantly high average root number and root length was achieved in full strength MS medium accompanied with similar quantities for example BAP (1.5 μM), NAA (0.5 μM) and GA_3 (0.1 μM) combination. A separate medium for root initiation was not required. After 1 year of adaptation, a total of 91% survival of plantlets was recorded. Similarly, a rapid multiplication protocol of *V. wallichii* was established using shoot tip and axillary bud as explants (Mathur et al. 1988). Various other studies using different explants of *V. jatamansi* like shoot buds (Kaur et al. 1999), rhizomes and leaf (Das et al. 2013) were also established.

5.5.7.2 Preparation of the Field

Fields are well drained for cultivation of *V. jatamansi*. The soil of the field should be pulverized properly by plowing the field thrice before planting the species to obtain best rhizomes and roots production. The optimum period for first plowing is June month, and then during second plowing in the same month FYM at 20 t/ha should

Table 5.3 In vitro propagation method available for *V. jatamansi*

S. No.	Plant part	Medium	Hormone combination	Results	References
1	In vitro raised leaves	MS basal medium	(i) 1.0–7.5 μM 2,4-D and 5.0 μM NAA (ii) 5.0 μM IBA, 5.0 μM NAA or 1.0–5.0 μM 2,4-D	Embryogenic callus stimulated solely in the presence of auxins, namely 1.0–7.5 μM 2,4-D and 5.0 μM NAA and differentiated into adventitious shoots and somatic embryos, respectively, when placed in the same medium	Chen et al. (2014)

(continued)

Table 5.3 (continued)

S. No.	Plant part	Medium	Hormone combination	Results	References
2	Nodal explants	MS	Medium supplemented with 1.5 μM BAP, 0.5 μM NAA and 0.1 μM GA_3 Rooting Medium: 1.5 μM BAP, 0.5 μM NAA and 0.1 μM GA_3	Medium supplemented with 1.5 μM BAP, 0.5 μM NAA and 0.1 μM GA_3 exhibited maximum mean shoot length, shoot number and leaf number. A hundred percent rooting with considerably maximum average root number (27.5 ± 1.98) and root length (50 ± 1.35 cm) was obtained in full-strength MS medium accompanied with same concentration of BAP, NAA and GA_3. A total of 91% plantlets survived after 1 year of acclimatization	Purohit et al. (2015)

(continued)

Table 5.3 (continued)

S. No.	Plant part	Medium	Hormone combination	Results	References
3	Shoot tip and axillary bud explants	MS medium	MS medium comprising Kn or BAP (5.0 mg/L) in combination with IAA (1.0 mg/L)	MS medium containing Kn or BAP (5.0 mg/L) in combination with IAA (1.0 mg/L) induced an optimal growth of shoots within 6–8 days from both apical and axillary bud explants. The roots developed on the same medium within 2–3 weeks. Hardening of in vitro grown plantlets in pots under glass-house conditions was dependent upon the temperature and humidity. A cold-temperate climate favored early establishment.	Mathur et al. (1988)

(continued)

Table 5.3 (continued)

S. No.	Plant part	Medium	Hormone combination	Results	References
4	Shoot buds	Solid medium	BA alone or in combination with IAA or NAA	Rapid and large-scale propagation of *V. jatamansi* by stimulation of shoot production from shoot buds was established. The sterilized explants were established on solid medium supplemented with BA alone or in combination with IAA or NAA. The buds cultured on nutrient medium supplemented with BA and IAA or NAA formed shoots, which after 3-4 weeks produced roots on the same medium. Survival of 100% was recorded on acclimatization and field establishment of well-rooted shoots	Kaur et al. (1999)

(continued)

Table 5.3 (continued)

S. No.	Plant part	Medium	Hormone combination	Results	References
5	Rhizomes, leaf	MS medium	Different amount of 2,4-D, NAA and IBA on callus stimulation and production of valepotriates	The callus stimulation frequency was detected to be optimum in rhizome explants on media supplemented with 0.5 mg/L 2,4-D. MS medium fortified with 0.75 mg/L thidiazuron in combination with 0.5 mg/l NAA exhibited the maximum regeneration frequency (88.6%) and generated the highest shoot buds number (15.20 ± 0.20). Vigorous callus observed from MS medium supplemented with diverse concentrations of 2,4-D, NAA and IBA were used for industrially important valepotriates (acevaltrate, valtrate and didrovaltrate) analysis. HPLC evaluation of callus showed that medium with 2, 4-D (1 mg/L) was increased acevaltrate and didrovaltrate yield, whereas valtrate production was higher in case of medium supplemented with NAA (1 mg/L).	Das et al. (2013)

be mixed in the soil. The soil was made friable using final plowing (NMPB 2008; Mukherjee 2015).

5.5.7.3 Transplantation and Geometry of the Plant

August month is observed appropriate for seedlings transplantation (height 8-10 cm) from nursery to the ground. Maximum rhizome yield can be obtained by keeping the spacing between rows about 40–45 cm while in a row it should be 30 cm amidst plants (Slathia 2005). Plantation of the seedlings of species into hills in mid of August demonstrated by higher growth and below ground biomass. Below-ground biomass production of *V. jatamansi* is influenced by distance as spacing requirement of a specific species can hamper its production in different stages (Mukherjee 2015). The findings from this research exhibited a suitable geometry of crop is vital throughout transfer, as it decreases plant competition for water, nutrient, requirement of space and light, and findings in best growth of biomass at its productive prospective.

5.5.7.4 Cultivation in Different Agroforestry System

V. jatamansi is medicinal plant found to have shade loving nature and detect to accompanying with forest trees in nature. Therefore, this species possess enormous possibilities in agroforestry. Various trees species like *Robinia pseudoacacia, Acacia mollissima*, (Singh et al. 2010), *Grevillea robusta, Jacaranda acutifolia, Bauhinia variegata* and *Morus alba* (Vats et al. 2002) are found to be associated with *V. jatamansi*. The plant is also observed to grow well under *Quarecus leucotricophora, Pinus roxiburgi and Rhododendron arboreum* canopy and open grassy habitat (Jugran et al. 2013a, 2018). Paquette et al. (2006) reported that the trees canopy in a forest create undergrowth microclimate for the improved growth of *V. jatamansi* (Paquette et al. 2006).

5.5.8 Nutrition

Soil fertility is an essential factor during development of *V. jatamansi*. Hence, use of FYM is recommended at different doses. It is generally found that Indian subcontinent soil has nitrogen deficiency than the other macronutrients. Thus, the use of inorganic fertilizer, i.e., N, P & K at the scale of 150, 75 and 75 kg/ha was suggested for proficient crop (Singh et al. 2000). In contrast, biofertilizer supplementation to the crop of *V. jatamansi* increases biomass by preserving soil nutrients and enhancing plant efficiency for more nutrient uptake (Slathia 2005). Different biofertilizers like phosphate solubilizing bacteria (PSB), azotobacter (Azoto) and VAM (Vesicular-arbuscular mycorrhiza) and their mixtures (10 kg/ha ratio) were used to treat the soil of *V. jatamansi* crop. Study revealed that plants treated with mixtures in the ratio

of 1:1:1 exhibited higher N, P, K. Similarly, underground rootstock, soil P and K exhibited positive corelationship with each other. Secondary metabolites (phenolics, flavonoids, tannins and antioxidants) development in control and mycorrhiza-treated *V. jatamansi* plants showed high level of these metabolites in treated plants (Jugran et al. 2015d).

5.5.9 Water Requirement

V. jatamansi crop does not need continuous irrigation practices. During summer season to obtain the optimum development and yield irrigation followed by day's break is suggested. However, appropriate moisture in soil is required immediately after transplantation for improved establishment. Slope and soil water holding capacity are most vital parameters to govern irrigation strategy which vary from 1 to 2 weeks. Herb from plantation to establishing period needed frequent irrigation. However, the irrigation in monsoon season is not required.

5.5.10 Plant Protection from Weeds

Prior to monsoon time, a lightly plowed field soil is highly beneficial to escape from weeds intrusion in both the years during plant development. Hence, uprooting annual grasses manually is beneficial for weeding beyond herbicides use. Studies suggested that weeding can be more appropriate within 30 days of field plantation of crop, and successive removal of weeds can be performed at a gap of 25–30 days (NMPB 2008). Before the field establishment of *V. jatamansi* plants, manual weeding needed to perform in the field plants to remove competition with invasive species. Species like *Ageratum conyzoides, Bidens pilosa, Cynodon dactylon, Plantago lanceolata*, other, grasses and sedges commonly observed are recorded in the crop of Indian Valerian at CSIR-IHBT, Palampur, India. However, in Uttarakhand at few places, *Azaratus adenophora* is also recorded (personal observation). Tissue culture-raised plantlets of *V. jatamansi* have been planted at Narayan Ashram, Pithoragarh, Uttarakhand, by G.B pant National Institute to promote and demonstrate the cultivation of *V. jatamansi* among farmers for their livelihood enhancement. Secondary metabolite of plant stimulates confrontation with pathogens and pests (Schmidt et al. 2008). The molds and pests are rarely caused any harm to the plants of the herb, for example, fungal infection, rhizome rot beneath water-logged situations. In case of such situation, 0.2% Dithane M-45 can be used to administer the plant soil, which prevents growth of the fungal spore (NMPB 2008).

5.5.11 Harvesting and Yield of Biomass

A study reported that during 1st year the yield of new root stock is 3.5–4.5 ton/hectare while it is nearly twofold in the 2nd year (7.0–7.5 ton/hectare). Thus, highest produce can be obtained by crop harvesting in 2nd year of plantation in month of July which is considered as favorable month to develop plant to attain highest length of shoots and root, else decrease in produce and quality is observed in July (Singh et al. 2010). Maximum volatile oil production was recorded in May month while it was lowest in October (Singh et al. 2010). On other hand, Rawat et al. (2017) observed highest volatile oil production in winter period and lowest in the spring period. Diverse developmental stages, namely preflowering, flowering and post-flowering samples from aerial and root parts of three natural populations located at an altitudinal gradient were evaluated Jugran et al. (2021). Qualitative and qualitative differences in essential oil obtained from rhizomes in diverse growth phenophases along the altitude were revealed. Maximum phenolics, flavonoids and antioxidant property in the root and aerial parts were recorded in post-flowering stage. The study concluded that post-flowering stage is suitable to produce maximum phytochemicals and antioxidant from *V. jatamansi*. Further, highest antioxidant property in flowering condition samples from higher altitude emphasized on the requirement of compound specific agroclimatic methods for commercial benefits from cultivation of this species. The production of enriched fraction of valepotriates is maximum in month of November or January of 2nd year (Singh et al. 2010). For *V. officinalis*, the optimum time for obtaining maximum valepotriates amount is February to March (Bos et al. 1998). This noticeably suggested the variations in the amount of chemical constituents in the context of season for specific species. Iridoids level in below-ground portion ranged from 2 to 5.6% in *V. jatamansi* while highest (8.0–12.0%) content of valepotriates in *V. edulis* of this genus was detected (Holzl 1975; Bos et al. 2002). These results also exhibited winter as the dormant period for *V. jatamansi* in which the amount of valepotriates demonstrated higher while the amount of essential oil increased throughout its dynamic growing period.

5.5.12 Management of Post-harvest Produce

Medicinal and aromatic plant (MAPs) crops management required suitable post-harvesting method. It involves handling, storage and other method of processing followed by mature crop harvesting helps to maintain the product quality for storage of a longer period. Some of the essential attributes determining superiority, e.g., color, moisture, active constituents and issues related to microbes are of serious concern with safety issue (Yahia 2006). Several parameters decreased the quality after crop harvesting if appropriate post-harvesting management practices are not followed. In case of storage conditions, most dominant post-harvest factors are relative humidity,

temperature, light, oxygen availability and atmospheric compositions which influence the quality of essential oil (Turek and Stintzing 2013). Among above-mentioned variables, most important factor is temperature which influence the products quality. Hence, the harvested material particularly rhizomes should be dried within 35–40 °C temperature. The options of deprivation of valepotriates constituents are higher above the mentioned temperature resulting in the formation of a yellow-colored compound known as baldrinals (Denee et al. 1979), which contain valtrate and acevaltrate isovaltrate (Hobbs 1989). In a study, valepotriates were not identified subsequently placing the sample at 36 °C for two weeks, as it degenerates rapidly in higher temperature and ultimately transformed into baldrinal, that comprises reactive constituents, namely acevaltrate and valtrate (Bos et al. 1996). The valtrate and acevaltrate are very responsive in nature and consequently can be utilized for polymers formation (Steinegger and Hansel 1992).

5.5.13 Genetic Diversity for Elite Identification

Studies are available on the genetic characterization, evaluation of genetic variations and elite identification of *V. jatamansi*. Genetic characterization of 7 morphotypes of the species was carried out using RAPD (Random amplified DNA polymorphic DNA) markers (Singh 2007). Similarly, analysis of six populations of Tagar was conducted by amplified fragment length polymorphism (AFLP) markers (Rajkumar et al. 2011) and displayed higher intra and low among population variations. Genetic variations of *V. jatamansi* gathered from 25 distant populations from Uttarakhand were investigated using ISSR & SSR markers (Jugran et al. 2013a, b, 2015a). The approaches using morphological, phytochemical and genetic variations data for elite identification and conservation of the elite *V. jatamansi* population and individuals were suggested (Jugran et al. 2016b, 2018). Likewise, several inter-simple sequence repeats (ISSR) makers associated with antioxidant property using analysis of molecular variance through locus-by-locus approach were identified (Jugran et al. 2013b). Similarly, ISSR markers linked with valerenic acid, phenolics and antioxidant properties were identified in this plant (Jugran et al. 2015b). Such studies are beneficial to identify suitable quality material for breeding as well as for large scale cultivation in the farmer's field.

5.6 Conclusions

In this review, we sought to project the clinical importance of *V. jatamansi* used traditionally in India and across the world. Researches on this herb highlighted particularly its pharmacological properties and secondary metabolites composition. Various disorders like diarrhea, stress, nervous complaints and gastrointestinal ailments are reported to be administered with *V. jatamansi*. However, authentication of the use of

species in such studies is needed to done by clinical trials for longer period. Further methods of cultivation and domestication of the species were also analyzed. As the herb is largely being utilized in multiple herbal mixture for formulation of diverse medicines and it is challenging to dedicate a specific remedial property is exclusively because of the constituents from this herb in the medicine, hence, it is important to measure bioguided isolation property to detect precise action of constituent. Besides, separation of metabolites and advancement in analytical tools of several in vivo and in vitro reports will carry several prospects to additionally decipher its potent biological properties. Moreover, existing research showed large intra- and inter-variations in the species or population; therefore, study should be focused on multiple locations/multi-populational samples to detect the effective molecule and new chemotypes. Moreover, the pharmacological investigations on this herb recommended its ability to be a potential source of drug for numerous diseases. Hence, strong clinical evidences, on this plant and constituents, would be critical for its protection and to assess the potential of the species to be used as a source of modern medicine. Although multiplication protocols for target species with 100% survival are reported, their genetic stability is also needed to be ensured not only comparing with few markers but in terms of their active constituents. For example, Himbala is a variety of *V. jatamansi* already developed by CSIR-IHBT Palampur which possesses high valeopotriates content. Recently, a new variety named as 'Him Surbhit' (CSIR-IHBT-VJ-05) has been developed by same institute comprises higher root biomass yield (3.40–4.50 tonnes/ha) and essential oil (0.29–0.31%) followed by two years of growth. Multi-location trials on species showed vigorous growth with higher adaptability in mid- and high hill regions (Pal et al. 2020). More new genotypes/population is needed to be explored for such varietal development. Further bisexual form of the species revealed higher biomass yield when cultivated in open environment. Therefore, emphasis is needed to be given on bisexual form for cultivation and breeding.

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