J. Orchid Soc. India, 34: 137-147, 2020 *ISSN 0971-5371*

ETHNOMEDICINAL STATUS AND PHARMACOLOGICAL PROFILE OF SOME IMPORTANT ORCHIDS OF UTTARAKHAND (NORTHWESTERN HIMALAYAS), INDIA

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Abstract

Orchids represent a highly established group of flowering plants, which are highly valued for their beautiful and long lasting flowers of different hues, shapes, and sizes. The orchid flora of Himalayan region is represented by 815 taxa in 137 genera including 116 endemic species. In Uttarakhand, the altitudinal and climatic variations from lower Shivalik to alpines support the growth of 68 genera and 238 species of orchids. They are grown as ornamentals and on the other hand, they are also used to cure a variety of human ailments. Infact, they are known for their medicinal usage especially in the traditional system of medicine and these plants are known to be used in many parts of the world in traditional healing system for treating a number of diseases since the ancient time. In the present communication, the data about the chemical constituents, pharmacological aspects, and indigenous uses of orchids of Uttarakhand, India has been compiled with a view to searching for the most effective medicinal orchids as a drug developing additive.

Introduction

ORCHIDS ARE amongst the most highly valued ornamental plants bearing the most beautiful and attractive flowers. Apart from their ornamental value, they are also recognised for their medicinal use, especially in traditional medicinal system (Devi *et al.,* 2018; Jalal *et al*., 2008; Kaushik, 2019; Pathak *et al*., 2010). They are highly established and economically valuable plants in the plant kingdom. In the past 120 years, orchids from the Himalayan region have been reported by a number of botanists (Kumar *et al.,* 2017, 2019; Kumar *et al.,* 2018; Mishra *et al*., 2018; Prakash and Pathak, 2019; Prakash *et al.,* 2018; Sharma *et al.,* 2017; Singh *et al.,* 2019). The Orchidaceae family is considered to be one of the largest, most diverse, and distinctive family amongst the angiosperms, with 28,484 species (Govaerts *et al*., 2017). In India, 155 genera and 1256 species contribute about 11.4 per cent of the Indian flora (Singh *et al*., 2019). About 815 species of orchid are estimated to be found in the Himalayan region (Singh *et al*., 2019). Moreover, a wide range of bioactive phytochemicals have been reported from orchids (Jhansi *et al.,* 2019; Joseph *et al.,* 2018). In fact, orchids are recommended for a variety of therapeutic uses in traditional medicine systems, such as *Ayurveda*, *Siddha*, and *Unani*, especially in India (Mishra *et al*., 2018). Due to topographical variation within short distances, various aspects of mountain slope and climate variation due to the influence of monsoon rain from East to West, the Himalayan region is suitable home for orchids (Bajracharya, 2001). In India, the distribution pattern of orchids follows the rainfall pattern (Mehra and Bawa, 1970). Orchids are found in several different habitats but not in places that are exceptionally cold all around the year. In Uttarakhand, the altitudinal and climatic variations from lower Shivalik to alpines support the growth of 68 genera and 238 species of orchids including 13 species endemic to the region (Singh *et al.,* 2019). Uttarakhand has been designated as the *herbal state* of India as it is a store house of many medicinal plants. There are many medicinal plants in the state; some of them have tremendous medicinal value (Jalal *et al*., 2008). The distribution of orchids is extremely patchy in the state of Uttarakhand (Bhandari *et al.,* 2018; Jalal and Rawat, 2009). The complex topography and climate conditions experienced within the state are related to a very rich biodiversity (Joshi *et al*., 2009). The difference in altitude and temperature from the lower Shivalik to the alpine promotes the development of 72 genera and 236 species of orchids (Khajuria *et al*., 2017).

The tubers of these plants are often used for medicinal purposes. However, the extreme risk of extinction due to over-exploitation and habitat loss is faced by many of these orchids (Mishra and Saklani, 2012; Pathak *et al*., 2010). Attempts have been made to develop

Received: October 20, 2020; Accepted: December 25, 2020

efficient protocols for mass propagation of some of these medicinally important species *in vitro* at Orchid Laboratory, Department of Botany, Panjab University, Chandigarh (Chauhan *et al.,* 2015; Pathak *et al.,* 2001, 2017; Vasundhra *et al.,* 2019; Vij *et al.,* 1995). However, as this number is negligible as compared to the total number of commercially important Indian orchids, much needs to be done in this direction in future. Moreover, these plants are important not only for their aesthetic value, but also known to act as ecological indicators. Their absence signals a shift in the region's soil and air quality (Joshi, *et al*., 2009). For the cultivation of medicinally and floriculturally important orchids, some areas in the state of Uttarakhand are considered ideal.

Keeping in view the above, presently an attempt has been made to compile the data about the chemical constituents, pharmacological aspects, and indigenous uses of orchids of Uttarakhand, India with a view to searching for the most effective medicinal orchid as a drug developing additive.

Some Medicinally Important Orchids of Uttarakhand and their Pharmacological Profile

A total of 10 medicinally important orchids from Uttarakhand have been analyzed for their chemical constituents, pharmacological profile, and their indigenous uses (Fig. 1).

Coelogyne cristata Lindl.

Coelogyne cristata, commonly known as *Hadjojen*, is an epiphytic or saxicolous orchid, *rhizome* rigid, 4-6 mm in diameter, *pseudobulbs* 1.5-3 cm apart on rhizome; *leaves* linear-lanceolate, *lamina* 10-17 × 0.7-1.9 cm; *inflorescence* heteranthous, 8-12 cm long, basal half embraced in *sheaths*; raceme 5-7 cm long, 2-10 flowered; *petals* similar to *sepals*, 9-11 mm wide, fruit *capsule* (Eflora; Teoh, 2016). The plant tends to grow in the East Himalaya, India (Assam), Nepal, Tibet, and the West Himalaya on large rocks and along forest margins (Eflora; Kew Science-Plant of the World Online, 2020).

Pharmacological Profile

Ethanolic extract (5, 10, and 20 $mgkg^{-1}$; b.w.) of *C. cristata* has been tested for osteoprotective activity in mice deficient in ovariectomized oestrogen. The results revealed that the extract showed significant osteoprotective effects with restoration of trabecular microarchitecture in both femoral and tibial bones and improved bone density; it was further devoid of any uterine estrogenicity at any of these doses. It was concluded that the ethanolic extract has the potential for post-menopausal osteoporosis treatment (Sharma *et al*., 2014).

Crepidium acuminatum (D.Don) Szlach.

Crepidium acuminatum, commonly known as *Jeevak*, is a terrestrial or lithophytic *herb* with succulent *stem*; *pseudobulbs* ovoid or oblong; *roots* clustered at base of *pseudobulb*, 1-2 mm thick; *leaves* 3, 4, spreading, membranous, ovate to ovate-lanceolate, acute or acuminate; *inflorescence* raceme, terminal, erect, 6-10 cm long; *flowers* yellow-green tinged, 10-12 mm across; *fruit* capsule, fusiform, ribbed (Teoh, 2016; Vij *et al*., 2013). The plant is located at an elevation ranging from 300 to 2100 m in forests such as pine or oak (Teoh, 2016). It is distributed across India including Andaman and Nicobar Islands, East and West Himalaya (Kew Science-Plant of the World Online, 2020).

Interestingly, it is used as an ingredient of *Chyavanprash* (an Ayurvedic rejuvenating tonic; Pathak *et al.,* 2010) and other formulations such as Ashtavarga churna, Rasayan, Ghrita, Gutika, Taila, Agada (Arora *et al*., 2017).

Pharmacological Profile

The antimicrobial activity of *C. acuminatum* pseudobulb extracts (chloroform, ethyl acetate, and ethanol) was assessed by disc diffusion method against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli,* and *Pseudomonas aeruginosa*. The results revealed that both extracts showed strong antimicrobial activity with inhibition zone diameter ranged between 6.5-20.0 mm (Arora *et al*., 2017). Methanol, acetone, chloroform, acetonitrile, and water extracts from leaves and stem of wild as well as *in vitro* derived plant extracts of *C. acuminatum* were evaluated for anti-oxidant activity by 2,2-diphenyl-1-picrylhydrazyl (DPPH), ferrous ion chelating, and 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical scavenging assays using ascorbic acid (5-100 μgml^{-1}), Ethylenediamine tetra acetic acid (EDTA; 10-200 μgml^{-1}), and trolox as positive controls. Amongst tested extracts, methanolic leaf extract from *in vitro* derived plants showed significant antioxidant activity with IC_{50} 42.66±1.8 μgml^{-1}, but it was lower than ascorbic acid (IC_{50} 38.24 ±2.5 μgml^{-1}). On the other hand, methanol stem extracts showed moderate DPPH scavenging effects where lowest radical scavenging potential was observed with aqueous stem extracts of wild plant (IC_{50} 178.56±2.9 μgml^{-1}). Moreover, methanolic leaf extract of *in vitro* derived plants exhibited a very strong chelating activity (83.8±3.4%) than other extracts, whereas the least activity was

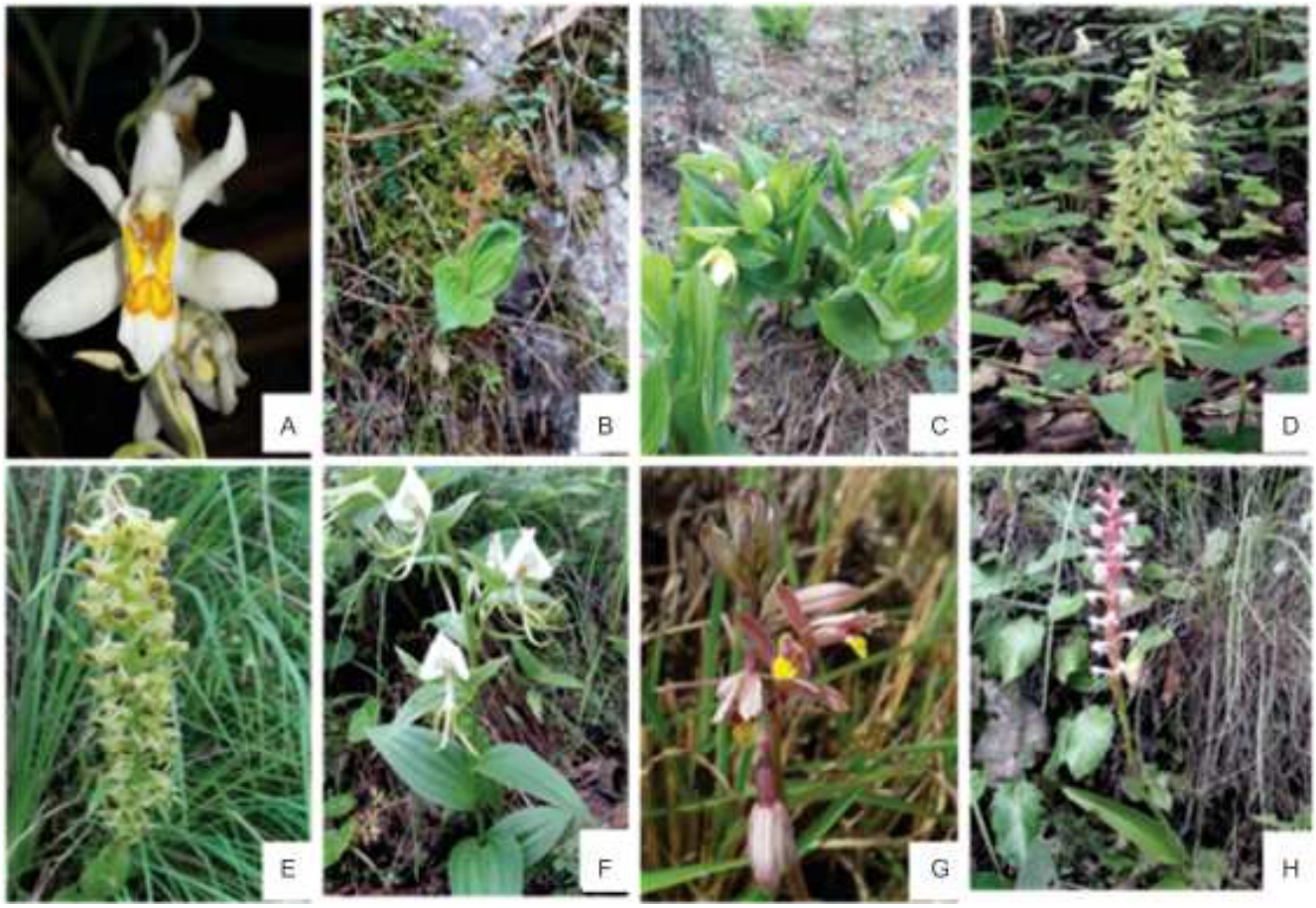

Fig. 1. A-H. Some of the medicinal orchids of Uttarakhand region of India: A, *Coelogyne cristata* Lindl.; B, *Crepidium acuminatum* (D.Don) Szlach.; C, *Cypripedium cordigerum* D.Don; D, *Epipactis helleborine* (L.) Crantz; E, *Habenaria edgeworthii* Hook.f. ex Collett; F, *Habenaria intermedia* D.Don; G, *Eulophia dabia* (D.Don) Hoch.; H, *Satyrium nepalense* D.Don.

shown by aqueous stem extract of wild plant (45.12±1.9%). On the other hand, a significant ABTS radical scavenging effect was observed in methanolic leaf extracts of tissue cultured plants with IC_{50} value of 13.32±1.1 µgml^{-1}, but it was lower than trolox (7.42±0.8 µgml^{-1}). These findings indicated a substantially greater capacity for free radical scavenging in the leaves of *in vitro* plants as compared to wild plants (Bose *et al*., 2017).

Cypripedium cordigerum D.Don

Cypripedium cordigerum is a large terrestrial *herb*, 50-80 cm tall, *roots* clustered on creeping *rhizome*, *stem* stout, *leaf* blade elliptic or broadly elliptic, 10-15 × 4-10 cm, sparsely ciliate, apex acute or acuminate; *inflorescence* terminal, 1 or rarely 2-flowered; *flower* solitary, 10 cm across; *petals* are droopy; dorsal *sepal* and *petal* greenish yellow, *lip* white (Teoh, 2016; Vij *et al*., 2013). It is known as *Jibri* in Nepal. It occurs in wet and shady areas, in open glades, *Pinus* forests, and grasslands throughout East and West Himalaya (Kew Science-Plant of the World Online, 2020; Teoh, 2016).

Pharmacological Profile

The ethanolic, methanolic, chloroform, and aqueous extracts of *C. cordigerum* (leaves, roots, and tubers) were evaluated using the agar well diffusion method for their antimicrobial activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Colistin was used as positive control against *S. aureus* (zone of inhibition 13 mm) and doripenam for the *P. aeruginosa* (14 mm). It was found that all the extracts at 100 mgml^{-1} showed activity against *S. aureus* with zone of inhibition ranging between 7-16 mm, while inhibition against *P. aeruginosa* ranging between 7-15 mm (Bharal *et al*., 2014).

Dactylorhiza hatagirea (D.Don) Soó

Dactylorhiza hatagirea, commonly known as marsh orchid, is a temperate, alpine orchid, 30-90 cm tall, herbaceous, with paired *tubers*, numerous leaves near base; *leaves* lanceolate or oblong, blotched with purple, progressively smaller towards top; *inflorescence* up to 15 cm long, densely many-flowered; *flowers* resupinate,

purple to a flesh pink, yellow, and white, arranged around the rachis much like a hyacinth (Eflora; Teoh, 2016). The plant is mostly found throughout Himalayas in marshy open places and coniferous forests (Eflora; Kew Science-Plant of the World Online, 2020).

Pharmacological Profile

The antioxidant effect of the ethanolic extract obtained from underground sections of *D. hatagirea* were assessed using the DPPH scavenging process. It was found that the extract was found active with IC_{50} value of 97.40±7.3 µgml^{-1} (Kumar *et al*., 2010). The lyophilized aqueous extract obtained from the roots of *D. hatagirea* was evaluated in male albino rats for sexual activity and spermatogenesis. Aqueous extract was found to cause severe anabolic effects equivalent to testosterone therapy. In addition, the lyophilized extract greatly affected the behaviour of the treated animals that were more attracted to females, and a 2.5-fold increase in female attraction was observed ($p<0.01$) compared to a nearly doubled increase in attraction ($p<0.05$) in the rats treated with testosterone. Mount latency period, which during a sexual act is an indication of physical fatigue, was reduced in *D. hatagirea* treated group by 36 and 34 per cent in testosterone-treated group as compared to control group. This showed the efficacy of plants in enhancing and preventing sexual organ functionality and also helps to enhance sexual activity and performance (Thakur and Dixit, 2007).

Epipactis helleborine (L.) Crantz

Epipactis helleborine is an alpine, terrestrial orchid, 20-70 cm tall; *stem* glabrous toward base, becoming pubescent above; *leaves* 4-7, ovate-orbicular, ovate, or elliptic-lanceolate, lanceolate to linear-lanceolate, 3-13 × 1-6 cm, glabrous, apex acuminate to long acuminate; *inflorescence* raceme, loose to moderately dense, floral bracts spreading, linear to narrowly lanceolate, 10-70 mm long, exceeding flowers; *flowers* 15-50, small, *calyx* greenish, suffused with purple, lateral calyx 10-13 × 5-6 mm, apex oblique, corolla ovate, pale green, pink, purple or yellowish, 9-11 × 4-6 mm, *lip* indistinctly veined, constricted at middle into 2 parts, proximal part purplish to brownish, deeply concave, 9-12 × 8 mm, distal part recurved, pink, *column* 3-6 mm long, ovary glabrous; *fruit* capsules, obovoid, 9-14 mm long, glabrate to densely pubescent (Eflora; Teoh, 2016). It is locally known as *Trindrya* (Pande *et al*., 2006). The plant is found in moist to dry, rocky, shaded areas, deciduous mixed forests, cedar swamps, and forested streams, at an altitude up to 1300 m (Eflora). Its native range is from NorthWest Africa, Europe to China (Kew Science-Plant of the World Online, 2020).

Pharmacological Profile

Mannose-specific lectins obtained from *E. helleborine* (EHA) leaves were evaluated for anti-viral activity. It was observed that EHA exhibited strong inhibitory effect against human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) in MT-4 cells, and also showed a marked anti-human cytomegalovirus (CMV), respiratory syncytial virus (RSV) and influenza A virus activity in HEL, HeLa, and MDCK cells, respectively. The EC50 of EHA against HIV ranged between 0.04-0.08 µgml^{-1}, which is about 3 orders of magnitude below their toxicity threshold. Also, EHA found to be potent inhibitors of syncytium formation between persistently HIV-1 and HIV-2 infected HUT-78 cells and CD4 + Molt/4 (clone 8) cells. Unlike, standard dextran sulfate, EHA did not interfere with HIV-1 adsorption to MT-4 cells and RSV and influenza-A virus adsorption to HeLa and MDCK cells, respectively. It was concluded that, EHA was found highly effective in inhibiting HIV-1, HIV-2 induced cytopathicity in MT-4 cells (Balzarini *et al*., 1992).

Eulophia dabia (D.Don) Hoch.

Eulophia dabia, commonly known as *Misri,* is herbaceous, 16-45 cm tall; *pseudobulb* irregularly triangular or subglobose, 1-2 cm in diameter; emerging after anthesis, linear, 15-20 × 0.4-0.8 cm, gradually tapering at base into a *petiole*-like stalk; *inflorescence* racemose, 16-45 cm long, slender to stout; flowers pale pink to maroon, medium-sized, 18-25 mm in diameter, *pedicel* and *ovary* 11-22 mm, *calyx* 12-16 × 3-5 mm, oblong, apex acute or mucronate, lateral calyx slightly oblique, *corolla* 10-14 × 2-3 mm, narrowly obovate-oblong, slightly shorter than calyx, apex acute or mucronate; *fruit* capsule, 18 × 10 mm, pendulous, ellipsoid (Eflora; Teoh, 2016). In West Himalayan regions, plants tend to grow in grassy slopes and rocky wastelands.

Pharmacological Profile

Essential oil (3 mgml^{-1}) from aerial portion of *E. dabia* was tested against *Staphylococcus aureus*, *S. epidermidis*, *Escherichia coli*, *Klebsiella pneumonia,* and *Bacillus subtilis* for its anti-microbial activity using agar well diffusion assay. Streptomycin (2 mgml^{-1}) was used as standard with zone of inhibition 28 mm against *S. aureus* and *B. subtilis*; 29 mm against *S. epidermidis* and 30 mm against *E. coli* and *K. pneumoniae*. The results revealed that, oil exhibited activity against all tested bacterial strains except *S. epidermidis* with zone of inhibition ranged between 10 to 18 mm. The effect is more pronounced against *K. pneumoniae* (18 mm) (Nisar *et al*., 2013).

Table 1. Chemical profile, therapeutic, and ethnomedicinal uses of some orchids of Uttarakhand, India.

Botanical name	Chemical Constituents	Part used (Medicinal uses)	Therapeutic uses	References
Coelogyne cristata Lindl.	Coeloginin Coelogin	P (Cephalalgia, dyspepsia, epilepsy, fractures, nerve disorders, and pyrexia) Ps (Constipation, dysentery, and diarrhea)	Anti-aging, Anti-stress, Tonic	Majumder *et al*., 2001; Sharma *et al*., 2009; Pant, 2013; Sharma *et al*., 2014; Pramanick, 2016; Teoh, 2016
Crepidium acuminatum (D.Don) Szlach.	Diadzein Puerarin Tuberosin	Ps (Burning sensation, general debility, hematemesis, pyrexia, seminal weakness, and tuberculosis)	Aphrodisiac, Febrifuge, Refrigerant	Khare and Katiyar, 2012; Arora *et al*., 2017
Cypripedium cordigerum D.Don	Alkaloids Flavonoids Saponins	Rh (Mental disorders) L (Nervous disorders)	Aphrodisiac, Tonic	Sharma *et al*., 2009; Khan *et al*., 2012; Vij *et al*., 2013; Teoh, 2016; Barman *et al*., 2016
Dactylorhiza hatagirea (D.Don) Soo	Dactylorhins A-E	R and T (Burning sensation, burns, chronic pyrexia, cough, diarrhoea, dysentery, fractures. general debility, renal disorders, stomach ache, and wounds) T (Asthma, bronchitis and pulmonary disorders)	Aphrodisiac, Nervine	Basu *et al*., 2009; Pant and Rinchen, 2012; Pathak *et al.,* 2010; Wani *et al*., 2020
Epipactis helleborine (L.) Crantz	Mannose-specific lectins	T (Cephalalgia, gout, insanity, and stomach ache) R (Dentalgia, eye ailments, pharyngitis, and trauma)	Aphrodisiac	Balzarini *et al*., 1992; Pant, 2013; Teoh, 2016
Eulophia dabia (D.Don) Hoch.	Flavonoids Phenols	T (Cardiac disorders, scrofula, and worm infestation)	Appetizer, Aphrodisiac	Hossain, 2009, 2011; Dawande and Gurav, 2017; Pathak *et al.,* 2010
Habenaria edgeworthii Hook.f. ex Collett	Phenolics	T and L (Anorexia, asthma, burning sensation, cataplexy, cold, emaciation, general debility, gout, helminthiasis, hematemesis, hyperdipsia, insanity, pyrexia, and skin diseases)	Antioxidant, Aphrodisiac, Appetizer, Anthelmintic	Dhyani *et al*., 2010; Rawat *et al*., 2014; Teoh, 2016
Habenaria intermedia D.Don	Alkaloids Gallic acid Scopoletin	T (Anorexia, arthritis, asthma, burning sensation, cough, general debility, gout, insanity, leprosy, myalgia, pyrexia, sciatica, and skin diseases)	Tonic, Expectorant, Rejuvenator	Balkrishna *et al*., 2012; Habbu *et al*., 2012; Rawat *et al*., 2014; Teoh, 2016
Spiranthes sinensis (Pers.) Ames	Spiranthols A-B Sinensols A-H. Spirasineol-A	P (Cephalalgia, chronic dysentery, epistaxis, hemoptysis, meningitis, and sexual dysfunction)		Shie *et al*., 2020; Teoh, 2016
Satyrium nepalense D.Don	Quercetin	T (Dysentry and malaria)	Aphrodisiac, Tonic	Bhatnagar *et al*., 2017; Teoh, 2016

P, Plant; R, Roots; Rh, Rhizome; Ps, Pseudobulbs; T, Tuber; L, Leaves.

Habenaria edgeworthii Hook.f. ex Collett

Habenaria edgeworthii is a perennial, terrestrial *herb*, up to 50 cm tall, with rather small, sessile tuberoids; *stem* leafy, somewhat flexuous; *leaves* 3-4, sheathing, second largest, 6-10 × 4.5 cm; *inflorescence* cylindrical; *flowers* yellow and green, deflexed in bud (Eflora). It is known as *Riddhi* in Hindi, Kannada, Malayalam, Tamil, and Telugu languages (Vardhana, 2013). The species is found in the East Himalaya, Nepal, Pakistan, Tibet, and West Himalaya in grassy pastures, open places, and oak forests at an altitude up to 3000 m (Eflora; Kew Science-Plant of the World Online, 2020). Interestingly, in Ashtavarga, it is an essential herb part (Teoh, 2016).

Pharmacological Profile

The anti-oxidant potential of *H. edgeworthii* methanolic extract was investigated using ABTS, DPPH, and FRAP assay. In ABTS radical scavenging assay, the extract showed significant ($p<0.01$) antioxidant potential

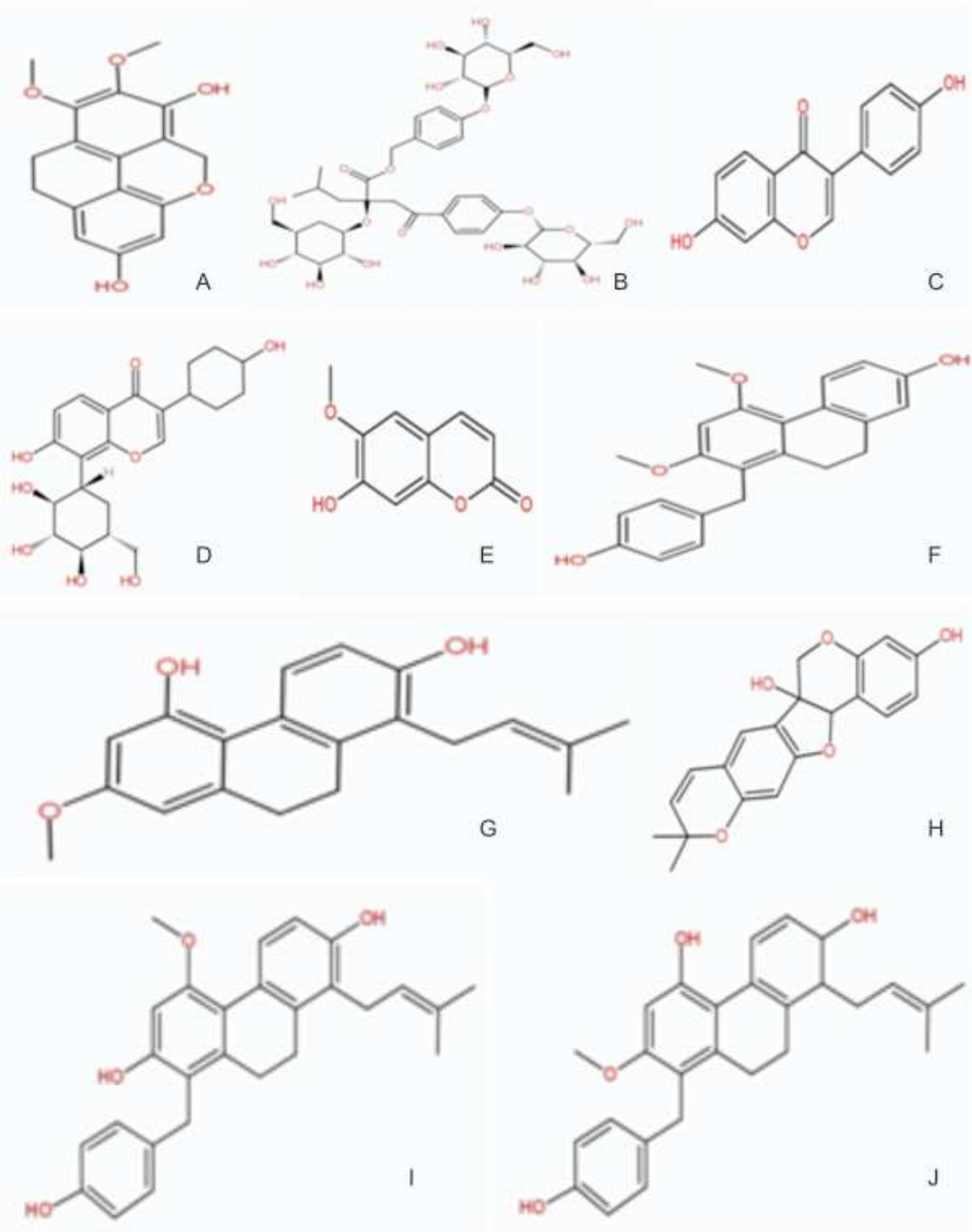

Fig. 2. A-J. Chemical structures of some bioactive compounds from some medicinally important orchids of Uttarakhand: A, Coelogin; B, Dactylorhin A; C, Daidzein; D, Puerarin; E, Scopoletin; F, Sinensol A; G, Spiranthol A; H, Tuberosin; I, Sinensol C; J, Spirasineol A.

(1.709 mM AAE/100g dry weight). On the other hand, antioxidant activity in other two methods was <1.5 mM AAE /100g dry weight (Rawat *et al.,* 2014).

Habenaria intermedia D.Don

Habenaria intermedia, commonly known as *Vriddhi,* is a terrestrial *herb*, up to 30 cm tall; with ellipsoid, fleshy *tuber*, 1.5-3 × 1-2 cm; *stem* erect, terete, stout; *leaves* 3.5-8 × 2-4 cm, ovate-lanceolate, base amplexicaul, apex acute; *inflorescence* raceme, 1-4 flowered; *flower* white or greenish, *calyx* ciliate, *corolla* erect, 2.2 × 0.8 cm, white, subovate-falcate, margin ciliate, unlobed, apex acute, stigmas clavate; *fruit* capsule, fusiform, beaked (Eflora; Vij *et al*., 2013). This orchid usually occurs in forests at an altitude up to 3000 m (Eflora). It is a native to East Himalaya, India (Assam), Myanmar, Nepal, Pakistan, Tibet, and West Himalaya (Kew Science-Plant of the World Online, 2020).

Pharmacological Profile

Ethanol extract (300 and 600 $mgkg^{-1}$; b.w.) of *H. intermedia* was evaluated for immunomodulatory activity by delayed-type hypersensitivity response (DTH), hematological parameters, and using carbon clearance assay in Swiss albino mice. Cyclophosphamide (20 $mgkg^{-1}$; b.w.) was used as a standard drug. Treatment with both doses increased response in foot pad edema significantly ($p<0.05$) when compared with control and standard group in DTH model. Moreover, administration of extract at both doses showed statistically significant ($p<0.05$) increase in RBC and WBC count as compared to standard and control treated mice. Also, in carbon clearance assay, phagocytic index was increased and statistically significant ($p<0.05$) when compared to phagocytic index (0.9488) of control and standard groups. The extract is a promising drug with immunostimulant properties (Sahu *et al*., 2013). Ethanol (EtHI) and ethyl acetate (EAHI) extracts from *H. intermedia* tubers were evaluated for *in vitro* anti-oxidant activity using DPPH, hydroxyl radical, and lipid peroxidation (LPO) assays. EtHI and EAHI showed DPPH scavenging activity with IC_{50} values 35.46 and 32.88 μgml^{-1}, respectively as compared with ascorbic acid (2.94 μgml^{-1}). Also, EtHI and EAHI inhibited LPO with IC_{50} 122.62 and 42.75 μgml^{-1}, respectively. On the other hand, EtHI and EAHI scavenged hydroxyl radical with IC_{50} 52.38 and 11.28 μgml^{-1}, respectively as compared with standard mannitol with IC_{50} 4.99 μgml^{-1} (Habbu *et al.,* 2012).

The anti-microbial potential of different extracts (aqueous, methanol, ethanol, acetone, and hexane) from *H. intermedia* tubers was evaluated using agar disc diffusion method against *Bacillus subtilis*, *Staphylococcus aureus*, *Micrococcus luteus*, *Escherichia coli*, *Aspergillus flavus*, *A. fumigatus*, *Microsporum gypseum,* and *Candida albicans*. Vancomycin, ciprofloxacin, ampicillin, and streptomycin were used as positive control against bacterial strains, while ketoconazole and fluconazole against fungal strains. The results revealed that, ethanol extract showed maximum activity against *E. coli* (11 mm), *B. subtilis* (11 mm) and *S. aureus* (9 mm) at 10 mg/disc concentration while, *M. luteus* was found to be most sensitive towards acetone extract. On the other hand, *A. flavus* and *A. fumigatus* showed sensitivity against hexane extract (Rawat *et al*., 2016).

Spiranthes sinensis (Pers.) Ames

Spiranthes sinensis is a small terrestrial orchid, 13-30 cm tall; *roots* 2-3 mm in diameter; *leaves* 2-5, erect and spreading, *lamina* 3-10 × 0.5-1 cm; *inflorescence* erect, 10-25 cm, glabrous; *rachis* 4-10 cm; *floral bracts* ovate-lanceolate; *flowers* purplish red or pink; *ovary* 4-5 mm including *pedicel*, dorsal *sepal* forming hood with petals, *petals* rhombic-oblong, oblique; *lip* 4-5.5 × 2.5 mm; *disc* papillate; *column* erect, 2 mm; *anther* ovoid; *stigma* discoid, weakly 3-lobed (Eflora). It is commonly known as Chinese spiranthes (Shie *et al*., 2020). *S. sinensis* grows both in acidic and alkaline soils, in lowland areas, meadows, woods, along roadsides, disturbed areas, and preferring a moist climate to a dry environment (Teoh, 2016). Its native range is India (Assam) to South Central Japan and New Caledonia (Kew Science-Plant of the World Online, 2020).

Pharmacological Profile

Phenanthrene derivatives: spiranthol-A, spiranthesol, spirasineol-A, orchinol, spiranthoquinone, and sinensol-C isolated from *S. sinensis* were evaluated for anti-adipogenic activity against intracellular lipid accumulation in 3T3-L1 adipocytes and further assessed for its mechanism of action. It was observed that, compounds: spiranthesol, spirasineol-A, and sinensol-C inhibited lipid accumulation with IC_{50} 38.9, 31.4 and 12.67 µM, respectively. On the other hand, other compounds showed activity with IC_{50} >60 µM when compared with standard curcumin (IC_{50} 33.66±0.95 µM). Furthermore, sinensol-C (20 µM) treatment significantly ($p<0.001$) decreased the relative mRNA expression of peroxisome proliferator-activated receptor γ (PPARγ), sterol regulatory element binding protein-1 (SREBP-1c), fatty acid binding protein 4 (FABP4) at day 3, 6 and 9, CCAAT/enhancer binding protein α (C/EBPα) mRNA level at day 6 and day 9, fatty acid synthase (FAS) at day 3 and 9 and adiponectin at day 9 as compared to untreated cells. Likewise, sinensol-C (5, 10, and 20 µM) significantly ($p<0.05$)

decresaed adipogenesis-related protein expression in 3T3-L1 adipocyte such as PPARγ, C/EBPα, SREBP-1c, FAS, and FABP4 with increased adiponectin protein level as compared to untreated cells. Adding on, sinensol-C (20 µM) and AICAR [an activator of adenosine monophosphate-activated protein kinase (AMPK): 1 mM] treatment significantly ($p<0.05$) enhanced phosphorylation of AMPKα, AICAR also significantly blocked PPARγ, C/EBPα, and SREBP-1c protein expression by 0.44, 0.46, and 0.33 fold, respectively in 3T3-L1 cells. It was concluded that, sinensol-C regulates adipogenesis via down-regulation of adipogenic transcription factors and up-regulation of AMPK and might have the capacity to modulate adipogenesis (Shie *et al*., 2020).

Satyrium nepalense D.Don

Satyrium nepalense is a terrestrial, robust, leafy *herb*, 20-70 cm tall; *tubers* oblong-ellipsoid to ellipsoid; *stem* 1-3 leaved, *leaves* usually basal and sub-opposite, ovate-lanceolate, or lanceolate-oblong, 4-19 × 2-5.5 cm; *peduncle* 6-30 cm, slender to stout; *rachis* 4-20 cm, *floral bracts* reflexed, ovate-lanceolate, 8-35 × 4-10 mm; *flowers* whitish, pink, or pale purple, dorsal *sepal* 4-6 × 1-1.8 mm, *petals* 3.5-5 × 1-1.2 mm; *column* incurved, 4-5 mm long (Eflora; Teoh, 2016). The plant is mostly found on bare slopes, at an elevation up to 1500 m in the Indian Subcontinent to East Central China (Kew Science-Plant of the World Online, 2020).

Pharmacological Profile

The anti-mycobacterial activity of different fractions (n-hexane, dichloromethane, ethanolic, and aqueous) of *S. nepalense* pseudobulbs, flowers, leaves, and stem was investigated against H37Rv and MDR strains. The results revealed that among tested samples, n-hexane flower fraction was the most active with minimum inhibitory concentration (MIC) 15.7 and 62.5 μgml^{-1} against H37Rv and MDR, respectively. On the other hand, standard rifampicin showed MIC 0.08 and 1 μgml^{-1}, respectively (Bhatnagar *et al.,* 2017). Further, the anti-leishmanial activity (*in vitro*) of above mentioned samples against promastigotes and amastigotes of *Leishmania donovani* was also evaluated. It was found that, the n-hexane fraction of pseudobulbs and flowers was the most active with IC_{50} 76.32±2.30 and 65.64±0.22 against promastigotes and 23.80±0.73 and 22.16±0.99 against amastigotes, respectively. Additionally, all extracts exhibited antibacterial activity against *Staphylococcus aureus*, *Enterococcus* sp., *Acinetobacter* sp., and *E. coli* with inhibition zone diameter ranged between 7.00±0.00 to 11.33±0.57 mm (Bhatnagar *et al.,* 2017).

Bioactive Compounds from Orchids

A vast range of bioactive constituents have been reported from various orchids, which are associated with broad spectrum biological activity. Moreover, amongst them, some have been found useful as drug developing additives. The alkaloids, dactylorhins, sinensols, and spiranthols are among the major bioactive constituents isolated from orchids. The chemical structures of representative chemicals have been depicted in Fig. 2.

Orchids as Therapeutics

The orchids were regarded as useful herbs, according to the Doctrine of Signatures, to cure a number of problems associated with fertility and virility. Several species are frequently listed for their therapeutic significance in ancient literature and continue to be used in local medicine to treat diseases such as nervous disorders, hypertension, gastrointestinal disorders, renal and musculoskeletal disorders, hepatic disorders, rheumatism, toothaches, dermal problems, tuberculosis, malignancy, dysentery, and miscarriage. Interestingly, some of them block the AIDS virus selectively. Salep, a highly nutritious drink having aphrodisiac and anti-diabetic properties, is prepared using the dried tubers of *Dactylorhiza hatagirea* (Vij *et al*., 2013). Orchids have been used for treating a variety of disorders including renal, gastrointestinal, and respiratory (Table 1).

Future Perspectives

The data on the traditional, ethnomedicinal, and pharmacological activities of some medicinally important orchids from Uttarakhand region was presented. All these orchids were reported to have different pharmacological activities such as antimicrobial, immunomodulatory, antioxidant, *etc.* Further, their therapeutic potential includes cure for gastrointestinal disorders and skin disorders; as aphrodisiac, tonic, and febrifuge *etc*. These have also recently been shown to be a rich storehouse of chemical components with promising anti-HIV and anti-adipogenic activity. However, there are apparent gaps in the studies carried out that need to be bridged in order to explore the full medicinal potential of orchids. These data showed encouraging evidence of the use of plants and their chemicals to help synthesize or formulate effective medication for curing different chronic disorders in the future. The orchids namely *Dactylorhiza hatagirea*, *Epipactis helleborine, Habenaria edgeworthii, Satyrium nepalense*, and *Spiranthes sinensis* have been recommended for a variety of therapeutic uses such as aphrodisiac, health tonic as well as in the treatment of sexual disorders. In order to make herbal formulations against sexual disorders and other

diseases, much needs to be learnt about these medicinally important orchids. Interestingly, these orchids have been used effectively in the treatment of many diseases with symptoms similar to coronavirus infection like fever, cough, breathing difficulties, and other respiratory disorders. There is an urgent need to plan future studies for developing efficient protocols for their rapid mass propagation (as their natural populations are on decline due to natural and anthropogenic factors in the ever shrinking habitats) and to study their efficacy as drug developing additives against coronavirus infection.

Acknowledgement

The authors (Acharya Balkrishna, Rajesh Juyal and Reema Devi) are grateful to Param Pujya Swami Ramdev Ji, Patanjali Yogpeeth, Haridwar for providing all the necessary facilities.

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