



## Therapeutic Potential of *Habenaria intermedia* D. Don: An Ayurvedic Herb for Combating Depression

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**Abstract:** Depression, a pervasive mental health disorder, stands as the foremost cause of mental health-related disability globally. Affecting millions of people at any life stage, including the elderly, depression is a potentially life-threatening condition that can erode one's hopes, ambitions, and even the will to live, thereby exerting a profoundly adverse impact on society. Clinical studies have brought to light serious concerns about recurrence rates, side effects, and drug interactions despite the fact that there are many pharmaceutical therapies for depression. The creation of all-natural antidepressant chemicals originating from different plant sources has attracted increasing attention in recent years. One such plant is *Habenaria intermedia* D. Don, commonly known as Vriddhi. This orchid family member is a vital component of the famed polyherbal rejuvenator Chyavanprasha. Traditionally utilized in various herbal medicines for its restorative properties, Vriddhi's rejuvenating qualities make it a promising candidate for depression treatment. The trend towards using plant-based medications is gaining momentum, with extensive research exploring their effectiveness in treating various ailments, including neurological disorders like depression. The natural substances extracted from these plants exhibit encouraging results as potential antidepressants. The rejuvenating properties of *Habenaria intermedia* D. Don suggest its potential as a natural antidepressant. As the demand for plant-based therapies continues to rise, further research into the efficacy and mechanisms of such herbal treatments will be crucial in developing innovative and effective solutions for combating depression and enhancing mental well-being.

**Key words:** - Anti-depressants, *Habenaria intermedia*, Phytochemicals, Vriddhi etc.

**Introduction:-** Depression is the main cause of mental health-related disability worldwide, making it a major global mental health concern. It often first manifests during mid- to late-adolescence, typically between the ages of 14 and 25, with a median 12-month prevalence rate of 4-5%. Major depressive disorder (MDD) negatively impacts relationships, careers, education, and can be linked to premature death, including through suicide, as well as obesity and cardiac illnesses. For individuals over 18 with comorbid physical health issues, depression's functional impacts are often more severe, complicating treatment<sup>1,2</sup>. Despite having fundamental clinical

characteristics, depression varies widely between individuals. Globally, an estimated 450 million people experience mental or behavioural illnesses, according to the World Health Report. This accounts for 12.3% of all illness cases globally. Major depressive symptoms are associated with alterations in brain monoamine neurotransmitters, including nor-epinephrine, serotonin, and dopamine<sup>3</sup>. Major depression is now the second most common cause of illness-induced disability worldwide, according to the World Health Organization<sup>4</sup>. According to WHO predictions, by 2030 depression will be the foremost contributor to the worldwide burden of diseases. After COVID, depression among population has increased many times. In 2020, the pandemic increased cases of major depressive disorders by 27.6 percent and cases of anxiety disorders by 25.9 percent worldwide, according to the COVID-19 Mental Disorders Collaborators conclusion<sup>5,6</sup>.

### **Pathophysiology of depression**

#### **Neurotransmitter Dysregulation**

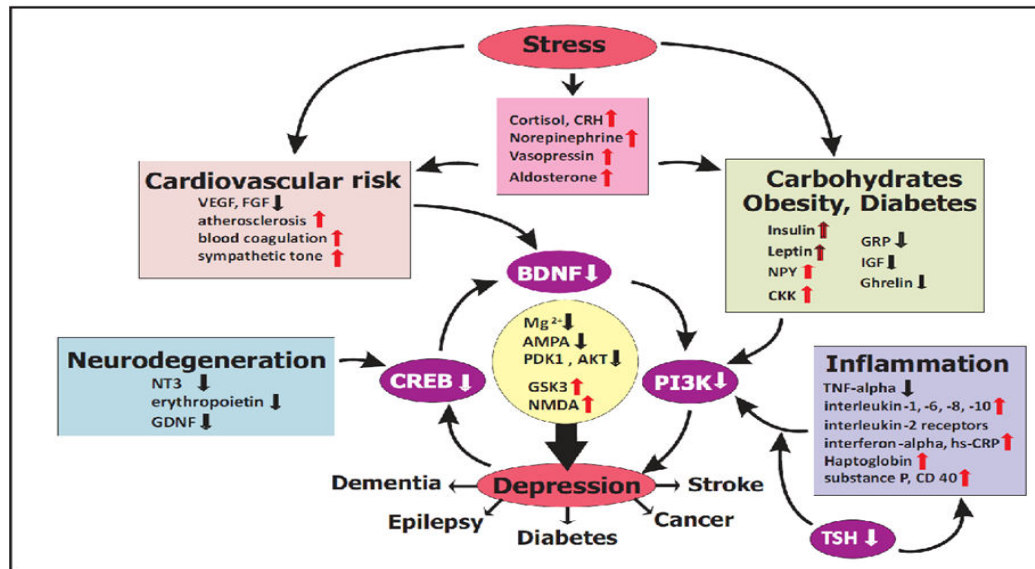
- **Serotonin:** Decreased levels of serotonin in the brain are linked to mood disturbances. Serotonin is synthesized from tryptophan and is involved in mood regulation, appetite, and sleep.
- **Norepinephrine:** Reduced norepinephrine activity is associated with decreased alertness and energy, contributing to the fatigue and lethargy seen in depression.
- **Dopamine:** Dysregulation of dopamine pathways can lead to anhedonia, the inability to feel pleasure, a hallmark symptom of depression.

#### **HPA Axis Dysregulation**

- **Cortisol:** Chronic stress can lead to hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, resulting in excessive cortisol production. Elevated cortisol levels can damage neurons, particularly in the hippocampus, and contribute to mood disturbances.
- **CRH and ACTH:** Increased levels of corticotropin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) are often found in individuals with depression, indicating HPA axis dysregulation.

#### **Neuroplasticity and Neurogenesis**

- **BDNF (Brain-Derived Neurotrophic Factor):** Depression is linked to decreased levels of BDNF, a protein that supports neuron survival, growth, and differentiation. Reduced BDNF can impair neuroplasticity and neurogenesis, particularly in the hippocampus.
  - **Synaptic Plasticity:** Chronic stress and depression can lead to synaptic atrophy, reducing the number and strength of synaptic connections, which affects cognitive and emotional function<sup>7,8</sup>.
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**Figure 1- Mechanisms leading to and resulting from depressive disorder**

Depression has become a global issue. Nowadays, depression has reached every person from small to old people<sup>9</sup>. Many allopathy medicines have been made to reduce depression. But these medicines have many side effects. Plants or herbs are a natural way to relieve depression. So, our study suggests that there is a natural way to cure depression without any side effects with the plant *Habenaria intermedia* D. Don commonly known as vriddhi.

### Herbs: As Anti-Depressants

During the past years, a major challenge is to understand the pathophysiology of depression. Studies mostly concentrate on more advanced and effective pharmacological therapies. There are several medications available to treat depression; however clinical examination of these medications has revealed relapse rates, adverse effects, and drug interactions. This has served as the justification for the creation of new antidepressants, including herbal remedies. The therapeutic chemicals used to treat many illnesses, including depression, have been derived from Indian medicinal plants and their derivatives. Due of their perceived safety and "natural" status, herbal products are frequently used. Ayurvedic herbal remedies have been the subject of more investigation recently because it is known that they help treat the conditions for which they have historically been used. Herbal therapy is an integral part of all traditional medicinal systems, including Siddha, Ayurveda, Naturopathy, Homoeopathy, Traditional Chinese Medicine, and Native American medicine. In recent years, there has been a lot of interest in the development of natural antidepressant chemicals that come from different plant sources<sup>10</sup>.

***Habenaria intermedia* D. Don:** -*Habenaria intermedia* D. Don, a member of the orchid family, commonly known as Vriddhi. It is found in the Himalayan Mountain nations of Pakistan, Bhutan, and Nepal, at an elevation of 2000–3300 metres above sea level. It is found in the Kashmir, Himachal Pradesh, Uttarakhand, and Sikkim regions of India's temperate Himalayas. Of the 600 varieties of *Habenaria* will (Orchidaceae) known to science, 100 species are found in India. *H. intermedia* has flavonoids, tannins, steroids, and coumarin glycosides, according to research. The species appears to be a significant source of antioxidants, hence providing a potent anti-free radical effect, because of the presence of phenolic compounds, such as gallic acid and hydroxyl benzoic acid<sup>11</sup>.



**Figure 2: - *Habenaria intermedia***

According to recent research, flavonoids may also have a beneficial effect on the way that human neuronal and neuroendocrine cell lines metabolise brain amines. Furthermore, flavonoids' antioxidant properties may prevent some brain diseases<sup>12</sup>. Unfortunately, to the best of our knowledge, not enough research has been done to investigate *Habenaria intermedia's* potential as an antidepressant modality. Perhaps the depressive action is due to flavonoids. Aphrodisiac, depurative, anthelmintic, and tonic in nature, the edible tubers are also pleasant and emollient. Tubers have the potential to help treat leprosy, skin problems, and asthma<sup>13,14</sup>. An essential part of the well-known polyherbal rejuvenator Chyavanprasha is this plant. Traditional uses for it include a variety of herbal remedies because of its restorative properties. From its rejuvenated effects we can say that it can be used for depression also<sup>15</sup>.

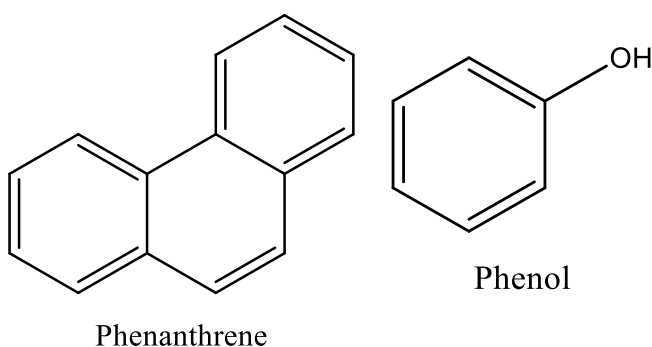
**Geographical source:-***Habenaria intermedia* is a species of orchid found in certain geographical regions. It typically grows in forested areas, grasslands, and meadows at elevations ranging from 1,500 to 3,000 meters above sea level. It prefers moist, well-drained soils and often thrives in areas with moderate to high humidity. It is predominantly found in the Himalayan regions of India in the states of Uttarakhand, Himachal Pradesh, Nepal, Bhutan, Tibet and parts of southwestern China<sup>16</sup>.

**Macroscopy:-**The morphology of *Habenaria intermedia* includes tuberous roots, an erect and slender stem, oblong to lanceolate leaves forming a basal rosette and scattered along the stem, and a terminal spike of greenish-white flowers. The flowers have distinctive three-lobed labellum and a long spur, adapted for attracting specific pollinators. This orchid species thrives in high-elevation, moist environments within the Himalayan region. It is a sturdy, perennial herb with a height of 25 to 50 cm. Stems are upright, cylindrical, terete, strong, and with leafy nodes. Three to five oval, oblong, or ovate-lanceolate leaves, dispersed, 5 to 10 cm long, sheathing, acuminate, base rounded or cordate, and 5-7 nerved. Flowers are scarce, far away, very large (5 cm across), white or greenish white, and borne in a raceme on a strong axis. Fruit pedicelled capsule, fusiform, beaked, terete, 3.8–5 cm long. Tuber sessile, oval or oblong, 1.5–3.5 cm long, 1.0–2.5 cm in diameter, covered in fine white hairs, circular at the other end but tapering towards the stem joint, skin is dirty, white, flesh is white. Fruiting occurs in September till October; flowering is from July to August. The edible tubers are pleasant and emollient<sup>17</sup>.

**Taxonomical Profile: -**

Kingdon	Plantae
Phylum	Streptophyta
Class	Equisetopsida
Subclass	Magnoliidae
Order	Asparagales
Family	Orchidaceae
Genus	Habenaria
Species	Habenaria intermedia

**Chemical Constituents: -** It has been demonstrated that genobiotic medicinal plants of the orchidaceae family have more therapeutic significance due to their varied chemical composition. Phenanthrene, bi-benzene, flavone, sterol, terpenes, and alkaloids are present in these members<sup>18</sup>. Total phenols, thiamins, tannins, and calcium all are present in significant concentrations in *H. intermedia*. Despite the fact that *Habenaria* species are utilized in traditional formulations, there are few scientific studies that support their therapeutic efficacy<sup>19</sup>.



**Ethnobotanical uses:-** Leprosy, asthma, skin disorders, depurative, aphrodisiac, and tonic properties are all attributed to the herb. It's a component of Chyavanprasha<sup>20,21</sup>. Different parts of the plant have been reported for its various medicinal uses:<sup>22,23,24</sup>

<b>Aerial parts</b>	Headache and abdominal pain.
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<b>Whole plant</b>	In gastric, hepatic and intestinal disturbances and as diuretic and emollient agent, abortifacient, antidiarrheal, to treat constipation and blood dysentery.
<b>Leaf</b>	Asthma, amenorrhea, dropsy, alcohol poisoning, rheumatism, vermifuge, decongestant, anti-inflammatory, against liver discomfort, kidney problems and in teething problems in children and in the treatment of skin and digestive disorders. It is used in burns, wounds, ulcers and chronic disorders such as HIV/AIDS.
<b>Tubers</b>	Rejuvenating, tonic, life span promoting and tonic.
<b>Fruits</b>	To relieve itching.

#### Plants with Anti-depressant Activity

A growing number of ailments, including neurological disorders like depression, are being studied for the potential benefits of plant-based therapies. It has been discovered that there are number of plants having antidepressant properties and are enlisted below:-

S.No.	Plant	Family
1.	<i>Agapanthus campanulatus</i>	Agapanthus
2.	<i>Akebiaefructus</i>	Lardizabalaceae
3.	<i>Albizziajulibrissin</i>	Fabaceae
4.	<i>Allium cepa</i>	Liliaceae
5.	<i>Asparagusracemosus</i>	Liliaceae
6.	<i>Bacopamonniara</i>	Scrophulariaceae
7.	<i>Carthamustinctorius</i>	Asteraceae
8.	<i>Cecropiaglazioui</i>	Cecropiaceae
9.	<i>Crocus sativus L.</i>	Iridaceae
10.	<i>Curcuma longa</i>	Zingiberaceae
11.	<i>Echinacea purpurea</i>	Asteraceae
12.	<i>Glycyrrhiza glabra</i>	Leguminosae
13.	<i>Hypericum perforatum</i>	Hypericaceae
14.	<i>Magnolia officinalis</i>	Magnoliaceae
15.	<i>Melissa officinalis</i>	Lamiaceae

16.	<i>Mondiawhitei</i>	Asclepiadaceae
17.	<i>Piper tuberculatum</i>	Piperaceae
18.	<i>Rhazystricta</i>	Apocynaceae
19.	<i>Salvia elegans</i>	Lamiaceae
20.	<i>Tinosporacordifolia</i>	Menispermaceae
21.	<i>Withaniasomnifera</i>	Solanaceae

**Table 1: - Plants with Antidepressant Activity**

The natural compounds isolated from the above-mentioned plants show promising results as potential antidepressants. Patient may be benefited greatly with the natural formulated multi component herbal formulation for the treatment of variety of neurological illnesses like anxiety and depression<sup>9,24</sup>.

#### **Pharmacological Profile: -**

**Immunomodulatory activity:** -The immunomodulatory activity of the ethanolic extract of *H. intermedia* tubers was assessed in mice using the carbon clearance assay and the delayed type hypersensitivity reaction, which measures an increase in foot pad thickness using vernier callipers. Foot pad oedema in the mice given ethanolic extract at doses of 300 or 600 mg/kg, p.o., responded more strongly. Comparing the ethanolic extract of *H. intermedia* at both doses to the conventional medication (cyclophosphamide 20 mg/kg) and control-treated mice, an increase ( $p < 0.05$ ) was observed in the RBC and WBC count. In comparison to the control and standard, it was discovered that the ethanolic extract of *Habenaria intermedia* exhibited considerable phagocytic activity at both doses. The activity could be attributed due to the presence of flavonoids, tannins, steroids, alkaloids and phenolic compounds<sup>25</sup>.

**Hepatoprotective activity:** -Gallic acid, the isolated component from the ethanolic extract of *H. intermedia* tubers, showed hepatoprotective effect against carbon tetrachloride-induced hepatotoxicity in albino rats when administered at a dose of 25 mg/kg, p.o., for seven days. Gallic acid produced a hepatoprotective effect in rats exposed to CCl<sub>4</sub>-induced liver damage by restoring blood protein levels to normal and lowering serum bilirubin, glutamic pyruvic transaminase (SGPT), and glutamic oxaloacetic transaminase (SGOT) levels to normal<sup>26</sup>.

**Anti-stress activity:** -The antistress activity of the ethanolic and ethyl acetate extracts of *H. intermedia* tubers was assessed in rats and mice using immobilization-induced acute stress, chronic stress, and swimming-induced stress experimental models, at doses of 100 or 200 mg/kg, p.o., and 200 mg/kg, p.o., respectively. In both acute and chronic stress situations, the test doses reduced the high levels of blood biochemical markers, including total cholesterol, triacylglyceride level, and serum glucose, and they also lessened the degree of ulcer index. The elevated adrenal weight in acute stress was decreased by pre-treatment with ethyl acetate and ethanolic extracts, whereas the adrenal weight was restored in chronic stress. In both acute and chronic stress, the thymus and spleen atrophy were reversed. Levels of ascorbic acid and cortisol contents in the adrenal gland were also restored<sup>27</sup>.

**Conclusion:** - The study successfully explored the antidepressant potential of *Habenaria intermedia*, a plant already recognized for its immuno-modulatory, rejuvenating, and various therapeutic properties. The investigation confirmed that *Habenaria intermedia* exhibits significant effects on the norepinephrine (NE) and serotonin (5-HT) receptor systems, which are

crucial in the treatment of depression. The results indicate that extracts from *Habenaria intermedia* can increase 5-HT neurotransmission, supporting its use as a potential therapeutic agent for depression. This finding opens new avenues for the development of novel antidepressant treatments derived from natural sources, providing an alternative to conventional synthetic drugs. Future research should focus on isolating specific active compounds within *Habenaria intermedia* and conducting clinical trials to further validate its efficacy and safety in treating depression.

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