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Potential Phytochemicals of *Smilax zeylanica* for Treatment of Brain Disorders

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ABSTRACT

Neurological disorders are described as conditions characterized by the systematic death of neurons. Conventional and newer molecules have been studied, but they only provide symptomatic benefits and come with a slew of adverse effects. The current vision will be the development of more convincing molecules that will interrupt the progression of such disorders. There are many synthetic drugs available, but they may cause a variety of other health problems. As a result, natural molecules derived from plants and other materials are being found to supplement existing medications. The WHO recommends that people increase their consumption of foods, herbs, and fibers as a way to lower their risk of neurodegenerative diseases. Chemically synthesized molecules can be replaced by phytochemicals from medicinal plants, which are a healthier and safer substitute. *Smilax zeylanica* contains polyphenols, flavonoids, phenolic compounds, tannins, alkaloids, and phenylpropanoids glucosides, according to phytochemical reports. The current article examines the effectiveness of *Smilax zeylanica*, a plant that could have therapeutic value for a variety of neurological disorders such as Parkinson's disease, Alzheimer's disease, Huntington's disease, convulsions, schizophrenia, and stroke.

Keywords: Neurological disorders, *Smilax zeylanica*, phytochemicals, anticholinesterase activity, antidepressant activity.

1. INTRODUCTION

Herbs are natural ingredients, and their chemical structure varies based on a variety of variables, resulting from variations from person to person, from active infusions to the use of herbal extracts in accordance with modern medicine's western methodologies. Traditional medicine has a strong tradition: it is the collection of procedures founded on myths, values, and traditions from various cultures and eras, which are mostly unexplained, and which are used in the protection of health, as well as the preventive, detection, development, and treatment of disease conditions. Traditional medicines have a basis of mystical or religious traditions, as well as common practice in every region, and the World Health Organization is working to define authoritative standards for clinical testing methods and the evaluation of traditional medicine's efficacy.[1,2]

Neurological diseases were the leading cause of disability-adjusted life-years (DALYs: 276 million) and the second leading cause of death worldwide

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in 2016. Between 1990 and 2016, the total number of deaths and DALYs from all neurological diseases rose (by 39 percent and 15 percent, respectively), while their age-standardized numbers declined (by 28 percent and 27 percent, respectively).[3]

The WHO recommends that people should increase their consumption of foods, herbs, and fibers as a way to lower their risk of neurological disorders.[4] There is a relevant product division that may lead to wellbeing in addition to the nutrients found in fresh fruits and green vegetables, such as fibre, carbenoids, and phytosterols.[5,6] Parkinson's disease, Alzheimer's disease, Huntington's disease, convulsions, schizophrenia, and stroke are among the most common health-care problems in developing countries, and they are a financial strain on the health-care system.[7]

Smilax is a genus of plant species, climbing and vines, also known as shrubs with creeping high branches that belongs to the monocotyledon Smilacaceae family. It contains around 350 species of herbaceous plants. Smilax species, which are found in tropical and subtropical areas, are widely used in herbal medicine from around globe, including Brazil, for the prevention of rheumatism and syphilis, as well as a diuretic.[8,9] *Smilax zeylanica* has been shown to be a food source for Asiatic elephants.[10]

Many other biological functions of Smilax species extracts already have been discovered, including anti-inflammatory, antinociceptive, antifungal, estrogenic, antiestrogenic, diuretic, and antihyperuricemic properties. Venereal infections, skin infections, cysts, burns, dermatitis, rheumatoid arthritis, swellings, and dysentery have all been treated with the herb in the past. Vegetables are made from leaves. The plant is used as a replacement for Sarsaparilla in many parts of the world. *Smilax zeylanica* has been identified as a possible substitute for the Ayurvedic drug Chopachinee. Diosgenin, trans-eugenol, β-sitosterol, smilagenin, sarsapogenin, hydroxyl-tyrosol, and squalene were among the chemicals found in the plant.[11-13]

The present review addresses the common applications, phytochemistry, and various neuro-pharmacological activities of *Smilax zeylanica* in this study.

2. PHYTOCHEMICALS IN SMILAX ZEYLANICA

Flavonoids, saponins, alkaloids, tannins, and phenylpropanoids glucosides were discovered in phytochemical tests.[14] By using repeated silica gel and Sephadex LH-20 chromatography, thirteen compounds were obtained from Smilax rhizomes using spectral analysis. They are kaempferol, dihydrokaempferol, dihydrokaempferol-5-O-P-D-glucopyranoside, vanillic acid, kaemperol-7-O-beta-D-glucopyranoside, kaempferol-5-O-beta-D-glucopyranoside, rutin, engeletin, isoengeletin, 3, 5, 4'-trihydroxystibene, 3, 5-dimethoxy4-O-beta-D-glu-copyranosylcinnamic acid, β-sitosterol, and β-daucosterol, respectively.[15]

Smilax zeylanica contains a wide range of chemicals and phytochemicals, according to research. Normal phytochemical studies, HPTLC, and GC-MS measurements have been used to identify phytochemicals such as alkaloids, tannins, triterpenoids, sterols, flavonoids, and compounds like diosgenin and β-sitosterol in the fruit.[11] Table 1 and 2 shows a number of phytochemicals and nutrients found in different parts of *Smilax zeylanica*.

3. ETHNOBOTANICAL USES

Plants are used for a variety of purposes by Indian herbal systems and ethnic groups around the world, including fruit, fodder, medication, dye, and building. *Smilax zeylanica* is historically used in India, Bangladesh, and Nepal. *Smilax zeylanica* tuber, stem, root, and leaves, used alone or in conjunction with other plants in some formulations (such as paste and decoction) to treat a variety of human and veterinary ailments around the world.[16]

4. NEUROPHARMACOLOGICAL ACTIVITIES

Several experiments on *Smilax zeylanica* have reported the plant's capacity for analgesic, antimicrobial, anthelmintic, anticonvulsant,

anti-inflammatory, cytotoxic, anti-oxidant, and hepatoprotective activities.

Table 1: Phytochemicals detected in *S. zeylanica*

Part	Phytochemical Compounds
Leaf	Glycosides, alkaloids, tannin, triterpenoids, sterols, steroids, flavonoids and saponins Hydroxytyrosol, trans-iso-eugenol and squalene
Root	Glycosides, phytosterols, tannins, seroids, phenols, flavonoids, diosgenin, and saponins
Rhizome	Glycosides, saponins, phytosterols, tannins, diosgenin, steroids, phenols, and flavonoids
Stem	Steroids, tannins, flavonoids and glycosides

Table 2: Nutrients detected in *S. zeylanica*

Nutrients	Quantity (mg/100g of DW.)
Nitrogen	610
Phosphorus	130
Potassium	300
Sodium	700
Calcium	838.8
Magnesium	226.8
Copper	2.56
Iron	29.92
Manganese	5.58
Zinc	2

4.1 *In Vitro* Antioxidant Activities

Uddin et al. (2015) discovered that petroleum ether and methanol extracts of *Smilax zeylanica* stems have antioxidant properties *in vitro*. Methanol extract showed marked behavior in all assays, as demonstrated by low IC_{50} values. There was direct link between antioxidant activity and flavonoid material.[14]

Thirugnanasampandan et al. (2009) discovered the ethanol, ethyl acetate, and chloroform extract of *Smilax zeylanica* leaves and stems had free radical scavenging and antioxidant properties. Overall, the anti-oxidant activity of ethanol extracts of leaf and stem was high. [17]

DPPH, ABTS, hydroxyl and superoxide radical scavenging assays, and reducing strength assays were used by Daffodil and Mohan (2017) to investigate the antioxidant ability of various solvent extracts of aerial sections of *Smilax zeylanica*. Methanol extract exhibited significant radical scavenging, as shown by low IC_{50} values.[18]

The ability of an ethanol extract of *Smilax zeylanica* leaves to scavenge DPPH radicals was investigated by Hossain et al. (2013). The extract scavenged DPPH radicals in a concentration-dependent manner, with an IC50 value of 30.93µg/ml.[19]

4.2 *In Vivo* Antioxidant Activities

In male rats induced with catalepsy by haloperidol, Ahemad et al. (2012) explored the anti-oxidant efficacy of root extract of *Smilax zeylanica in vivo*. Haloperidol treatment improved TBARS production while substantially lowering glutathione (GSH), superoxide dismutase (SOD), and catalase amounts. Treatment with extract significantly reduced these modifications to a degree that was almost natural.[20]

Rajesh and Perumal (2013) discovered that a methanolic extract of *Smilax zeylanica* leaves had *in vivo* antioxidant function in diabetic rats. In rats, streptozotocin caused an improvement in lipid peroxidation in the liver and kidney tissues, as well as a decline in the activity of antioxidant enzymes including SOD, catalase, glutathione peroxidase, glutathione reductase, glutathione-S-transferase, and non-enzymatic antioxidants including GSH, vitamin C, and vitamin E. Rats given the leaf extract, on the other hand, showed a noticeable improvement. In both liver and kidney tissues, the extract procedure reduced lipid peroxidation and normalized the activities of enzymatic and non-enzymatic antioxidants, suggesting potent *in vivo* antioxidant activity.

Rajesh and Perumal (2013) tested the *in vivo* antioxidant ability of *Smilax zeylanica* leaf extract in N-nitrosodiethylamine induced hepato-carcinogenesis in wistar albino male rats in another sample. The administration of extracts to rats resulted in a substantial decrease in lipid peroxidation and a significant rise in enzymatic and non-enzymatic antioxidants, all of which were severely compromised in hepato-carcinoma induced animals. They also discovered that *Smilax zeylanica* leaf extract has potent *in vivo* antioxidant function, decreasing the level of lipid

peroxidation and increasing the activities of enzymatic and non-enzymatic protection systems in mice treated with benzo(a)pyrene.[21]

Murali et al. (2010) found that methanol extract from *Smilax zeylanica* roots and rhizomes had *in vivo* antioxidant activity, suppressing lipid peroxide-tion and increasing the production of enzymatic antioxidants in albino rats given carbon tetrachloride.[22]

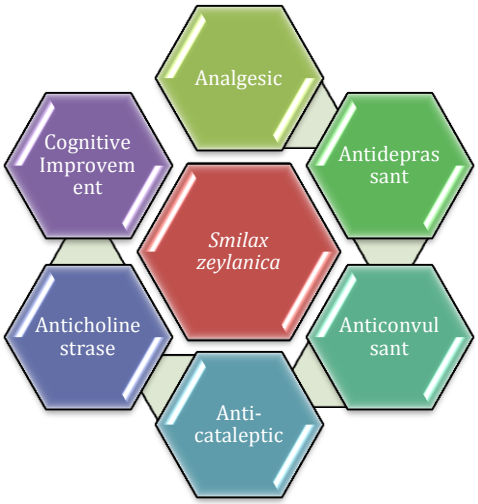

Fig. 1: Neuropharmacological effect of *S. zeylanica*

4.3 Analgesic Activity

Nithyamala et al. (2013) tested the analgesic efficacy of *Smilax zeylanica* root powder in albino mice using the hot plate procedure and the acetic acid mediated writhing method. In the hot plate process, oral administration of root greatly improved reaction time in a dose-dependent manner. Writhing produced by acetic acid was also inhibited by the root powder.[13]

Using Swiss albino mice, Jena et al. (2011) tested the analgesic efficacy of solvent extracts of *Smilax zeylanica* leaves using the tail immersion process. The administration of extracts resulted in substantial analgesia, which was similar to that of aspirin (standard drug). Methanolic extract has a strong analgesic effect overall.[23]

The analgesic effect of an ethanol extract of *Smilax zeylanica* Linn's leaves was described by Jena et al. (2011). The extract included reducing sugars, tannins, saponins, gums, hormones, alkaloids, and flavonoids, according to phytochemical study. In an acetic acid mediated writhing test in Swiss-Albino mice, the ethanol extract demonstrated statistically meaningful analgesic efficacy at doses of 250 and 500 mg/kg body weight. The findings point to the possibility that the extract contains chemical constituents that have analgesic properties.[24]

4.4 Anticonvulsant Activity

Jena et al. (2011) investigated the anticonvulsant effectiveness of *Smilax zeylanica* Linn, leaves in mice using experimental animal models. To monitor the extracts' anticonvulsant potency, albino mice were given strychnine-induced tonic convulsions. Both extracts decreased the triggered convulsions in mice. The ethyl acetate extract of *Smilax zeylanica*, in addition to other extracts, was found to have improved anticonvulsant efficacy.[24]

Madhavan et al. (2008) used pentylenetetrazole and maximal electro shock mediated convulsion models in swiss albino mice to assess the antiepileptic function of alcohol and aqueous extracts of *Smilax zeylanica* roots and rhizomes. Both extracts shortened the duration of the extensor process and the time it took to heal in maximal electro shock triggered seizures. Both extracts at 600 mg/kg greatly delayed the occurrence of convulsions in pentylenetetrazole-induced seizures.[25]

4.5 Antidepressant Activity

After two weeks of administration, Ahemad et al. (2016) measured the anti-depressive effect of *Smilax zeylanica* using the forced swimming test and tail suspension test methods. Monoamine levels in the striatum, cortex, hypothalamus, and hippocampus of mice, as well as MAO-A inhibition activity, were used to further investigate *Smilax zeylanica* Linn's anti-depressive impact. In both the FST and TST, *Smilax zeylanica* reduced mice's immobility time while also increasing 5-HT levels in the cortex, striatum, hippocampus, and hypothalamus, as well as norepinephrine levels. After two weeks of administration, *Smilax zeylanica* has an antidepressant-like impact. The antidepressant activity of *Smilax zeylanica* appeared to be mediated by an increase in monoamine levels.[26]

4.6 Anti-Cataleptic Activity

Ahemad et al. (2012) demonstrated the non-cataleptic potency of the ethanolic root extricate of *Smilax zeylanica* in haloperidol-induced catalepsy rats by measuring behavioral and biochemical parameters. Catalepsy was caused in male albino rats by giving them haloperidol (1 mg/kg, i.p.). In contrast to the haloperidol-treated group, all of the drug-treated groups showed significant reductions in cataleptic ratings, with the *Smilax zeylanica* (500 mg/kg) treated group seeing the largest reduction. As per the behavioral studies and biochemical calculations, *Smilax zeylanica* reversed haloperidol-induced catalepsy in rats. The antioxidant potential of haloperidol has helped to reduce oxidative stress and catalepsy caused by the drug.[27]

4.7 Anticholinesterase Activity

Yokeshwaran et al. (2020) investigated the anticholinesterase inhibitory function of *Smilax zeylanica* and *Smilax china* in animal models of neurodegenerative disorders such as Alzheimer's disease. Using animals and Ellman's procedure, the ethanolic and various extracts from the plant roots of *Smilax zeylanica* and Smilax china were screened for their acetylcholinesterase inhibitory action. At a concentration of 150 mg/kg, these extracts of *Smilax china* and *Smilax zeylanica* showed inhibitory actions (Cortex and Hippocampus), suggesting that they could be used to treat neurodegenerative diseases such as Alzheimer's disease.[28]

4.8 Cognitive Dysfunction

Senthil et al. (2018) looked into the impact of roots of ethanolic extract of *Smilax zeylanica* (EESZ) on the neuroprotective effects of aluminum chloride on rats' cognitive function. The hot continuous percolation process was used to remove the ethanolic extract from the roots of *Smilax zeylanica*. The latency of a passive avoidance task and the Morris water maze test were used to assess cognitive ability. The passive avoidance test revealed that the ethanolic extract from the roots of *Smilax zeylanica* at a higher dosage of 300 mg/kg of body weight substantially reversed the $AlCl_3$-induced reduction of cognitive function in rats. When compared to the control group, a higher dose of ethanolic extract from the roots of *Smilax zeylanica* greatly decreased escape latency in the Morris water maze. EESZ caused a substantial increase in latency time as compared to the control group, as shown by the EPM test. When compared to the control group, EESZ greatly reduced AChE occurrence in the rats' brain. The current study discovered that an ethanolic extract derived from the roots of *Smilax zeylanica* could have anti-disease Alzheimer's properties through behavioral, cognitive, and anti-AChE behaviors.[29]

5. FUTURE CONCERN

There are a number of medications that have been used to treat neurological diseases in the past, but they do not have the efficacy to slow disease development and often cause side effects. In recent years, various disease modifying methods have been identified, and various substances are being investigated as part of these strategies, but none of them has been effective in capturing the market. Several natural phytochemicals have been shown to have increasing effects in the treatment of a variety of neurological disorders. Phyto-chemicals include antioxidant, anti-amyloid, anti-inflammatory, anti-depressive, and anti-convulsing effects in addition to modulating the neurotransmitter function.

As a result, phytochemicals can be used to cure brain diseases in a variety of ways. There are few phytochemicals with toxic effects that have been released, despite the fact that more phytochemicals with negative effects need to be identified. It has been proposed that using natural phytochemical-rich plant extracts instead of prescription drugs in the treatment of neurological conditions is safer. However, only a few phytochemicals are widely used in medicine. Since phytochemical-rich plants are fostering hope in halting the development and progression of neurological disorders, it is critical to design clinical trials for such compounds that have not yet been entered into clinical trials.

6. CONCLUSION

This comprehensive literature search on *Smilax zeylanica* revealed that the plant is widely used ethnobotanically and has been shown to provide a broad variety of antioxidant and neuro-pharmacological activities. Traditionally, the plant has been used to cure diseases like piles, burns, venereal diseases, toothaches, and dysentery. Several sections of the plant have been shown to have antimicrobial, antioxidant, analgesic, anti-inflammatory, antipyretic, cytotoxic, hepatoprotective, and antidiabetic activity, according to studies. The existence of numerous phytochemicals and other phenolic compounds in the plant could account for the plant's pharmacological activities and therapeutic ability. Overall, the plant appears to be a promising candidate for the production of disease-specific therapeutic agents. In order to retrieve active concepts from the plant and examine their biological processes, further research is required.

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