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Plant & Its Derivative Shows Therapeutic Activity on Neuroprotective Effect

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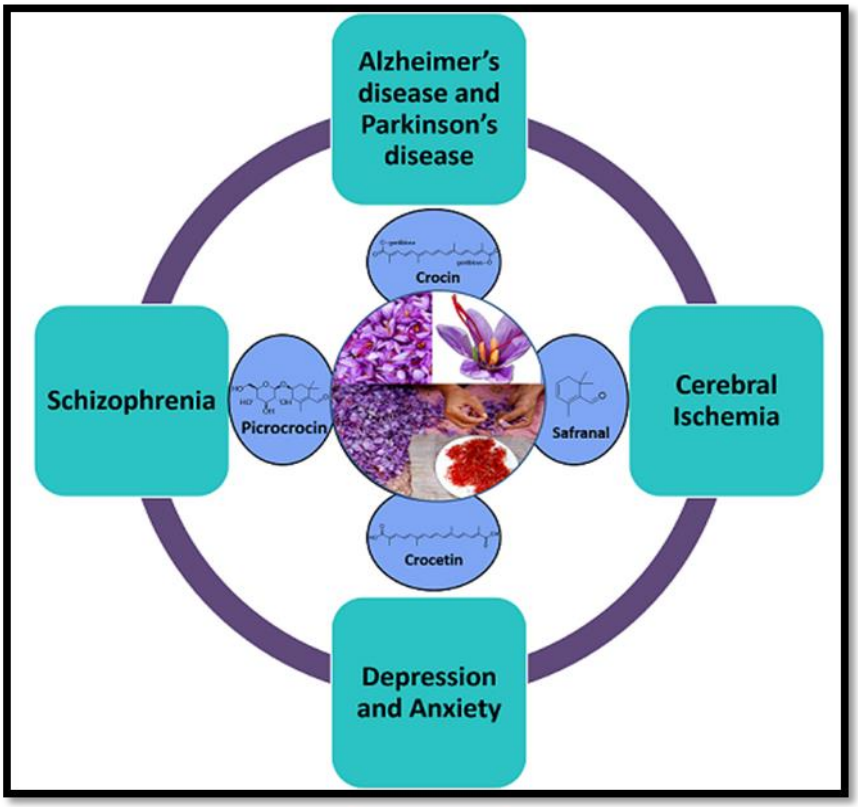
GRAPHICAL ABSTRACT



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ABSTRACT

In most cases, the death of neurons in certain parts of the brain is the defining feature of a condition that is classified as neurodegenerative. There have been studies conducted on both conventional and innovative drugs, however the results have shown that they only offer symptomatic advantages and come with a number of undesirable side effects. The finding of more potent compounds that can stop the pathophysiology of these diseases will be seen as a miracle in the present day. There is a wide variety of synthetic compounds accessible; nevertheless, these drugs may also create a broad range of additional health issues. As a consequence of this, scientists are looking to plants and other natural sources for the development of new medicines. In the practise of conventional medicine, it has been discovered that certain plants possess healing powers. The use of phytochemicals, which are produced from medicinal plants, may eventually replace the need for synthetic molecules. Numerous phytochemicals have been shown to be effective in the treatment of a wide range of diseases. This article discusses the potential therapeutic applications of plant-derived alkaloids for a number of neurodegenerative disorders (NDDs), including Alzheimer's disease (AD), Huntington's disease (HD), Parkinson's disease (PD), epilepsy, schizophrenia, and stroke. There are many different types of alkaloids that can be found in the plant kingdom. Some of these alkaloids include isoquinoline, indole, pyrroloindole, oxindole, piperidine, pyridine, aporphine, vinca, -carboline, methylxanthene, lycopodium, and erythrine byproducts. Alkaloids have a beneficial effect on the pathophysiology of these diseases because of their ability to act as muscarinic and adenosine receptor agonists, anti-oxidants, anti-amyloid and MAO inhibitors, acetylcholinestrase and butyrylcholinesterase inhibitors, an inhibitor of synuclein aggregation, dopaminergic and nicotine agonists, and NMDA antagonists.

Keywords- Herbal Plants, Phyto-chemical Study, Neuro-disease, Parkinson disease, Alzheimer disease.

I. INTRODUCTION

There is a correlation between serious and chronic depression and high rates of both death and morbidity. This potentially lethal mental disorder is one of the most serious causes of impairment in adulthood and is also one of the most common. Patients who suffer from chronic diseases have a significantly increased chance of acquiring depression, the percentage of which ranges from 22 to 46 percent. Even though the precise etiology of depression is still a mystery, it is believed that it is influenced by the complex interaction of a number of different hereditary components and the subsequent extensive exposure to environmental variables over the course of a lifetime. This illness has been shown to have a significant relationship with a number of factors, including those in the areas of psychology, genetics, and the environment. The development of this illness can be influenced by a variety of factors, including traumatic experiences, stress, and viral infections. Interactions between a person's environment and their genes appear to be a more accurate predictor of that person's likelihood of developing the disease than either the environment or the genes taken separately. Additionally, if epigenetic alterations are thought to be involved, early adversity may have had a part in the development of the disease. There is evidence that suggests a connection between structural and functional brain diseases and the hypothalamic–pituitary–adrenal axis, low levels of brain-derived neurotrophic factor, and glutamate-mediated toxicity.

Antidepressants that have been around for a while can be broken down into three primary groups: monoamine oxidase inhibitors, tricyclic antidepressants, and second-generation antidepressants. MAO inhibitors work to suppress the activity of the monoamine oxidase enzyme family. MAO inhibitors, such as tranylcypromine, phenelzine, and moclobemide, are frequently recommended to patients as the initial course of treatment. The blockage of the norepinephrine and serotonin transporter by MAO inhibitors results in increased synaptic c levels as well as an increase in the amount of neurotransmission. Tricyclic antidepressants are gradually being phased out in favour of newer medications that have less negative side effects. Some of the more recent second-generation antidepressants include serotonin–norepinephrine reuptake inhibitors, norepinephrine reuptake inhibitors, and selective serotonin reuptake inhibitors. In spite of the availability of these tried-and-true drugs, the majority of approaches made to treat depression have not been successful in bringing about clinical remission. This phenomenon can be explained due to the fact that there are many different systems involved in depression. Still today, a significant number of patients are unable to tolerate or respond to these drugs. The use of these medications is limited not only because they can have negative consequences, but also because their effects can be contradictory. Antidepressant medicines frequently cause a variety of unwanted side effects, including but not limited to anxiety, diaphoresis, tachycardia, tremor, drowsiness, inability to sleep, serotonin syndrome, parkinsonism, postural hypotension, and impaired vision.

Alternative treatments for depression have been the subject of a significant amount of research in recent years, with the goal of improving the therapeutic efficacy of these treatments. The use of plants as medicine is becoming an increasingly common substitute for conventional medications. In recent years, there has been a substantial amount of progress made in the research on the antidepressant properties of phytochemicals and medicinal plants. We conducted an open-ended and English-restricted search of MEDLINE

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(Pubmed) and Scopus using terms related to phytomedicine, phytochemical, herb, depression, and major depressive illness up until June 2022. Our search was limited to the English language. The focus of this review is on phytochemicals and herbs, specifically their potential to ease the symptoms of depression as well as prevent the onset of the condition. In addition to this, we explain how they function.

II. PLANTS WITH NEUROPROTECTIVE ACTIVITY

- ***Bellis perennis***

Bellis perennis is responsible for inhibiting the survival of neurons. When compared to a medium that was entirely composed of alcohol, there was a 90% decrease in the viability of the cells. Bellis perennis at concentrations of 2l/ml, 4l/ml, and 8l/ml were all made inactive. greater capacity of the cell to survive.

- ***Calendula officinalis***

The rats were administered MSG in addition to the extract of Calendula officinalis (COE). After receiving an injection of MSG for an hour, adult Wistar rats were given 100 and 200 mg/kg of COE to study its effects. After the treatment had been carried out to its conclusion, the mice were put to death and their locomotor activity was analysed in order to do additional research into the levels of LPO, GSH, CAT, TT, and GST. After that, the brains of the mice were extracted and examined. MSG had an influence on the behaviour of the animals, as well as their oxidative defences (LPO and nitrite), and the neuronal histology of their hippocampi. The adverse effects of MSG on behaviour, oxidative stress, and hippocampus damage can be mitigated by the supplementation of COE. For the purpose of this study, rats were used as research subjects to evaluate the neuroprotective effects of COE on 3-NP-induced neurotoxicity. The behavioural abnormalities, oxidative stress, and damage to the striatum in the rats' brains were recorded. Following the administration of the vehicle or COE (100 and 200 mg/kg) for a period of seven days, Wistar rats were subsequently given 3-NP at a dose of 15 mg/kg intraperitoneally. Following treatment, a person's short-term memory as well as their sensorimotor abilities were evaluated. In this study, the levels of glutathione, glutathione S-transferase (GST), catalase (CAT), and nitrite in brain homogenates were analysed. In order to investigate the full scope of the striatal neuronal damage, brain slices were analysed. The animal behaviour, antioxidant levels, and oxidative defence systems were all altered as a result of 3-NP (LPO, nitrite). a reduction in the total number of cells seen in the striatum. Because of its anti-oxidant qualities, COE has the potential to mitigate the behavioural issues, oxidative damage, and neuronal death that are brought on by exposure to 3-NP.

- ***Carthamus tinctorius***

HSYA demonstrates neuroprotective effects in rat cortical neurons against the neurotoxicity caused by glutamate. As a result of HSYA, there was a decrease in neurodeath. HSYA was successful in lowering Bax while maintaining a satisfactory protein to carbohydrate ratio. HSYA was successful in preventing NMDA from producing an excessive amount of NR2B. Plants such as astragali, ligusticum wallichii, angelica sinensis, and carthamus tinctorius have been shown to slow or stop the progression of neurodegenerative disease. When there is more blood flowing to the brain, patients suffering from Alzheimer's disease and Parkinson's disease experience an improvement in their symptoms. Neuronal protection afforded by the actions of hydroxysafflor yellow A (HSYA). After giving HSYA to male WKY rats with MCAO, the brain damage of the animals was examined after the administration of the compound. Evidence of infarction could be seen in slices taken from the brain. HSYA protects embryonic cortical cells from glutamate and cyanide injury (NaCN). When HSYA was administered to rats at a dose of 3.0 mg/kg, both the severity of neurological impairment and the size of infarcts were significantly reduced. Imodipine is 0.02 percent HSYA. The neuroprotective dose of sublingual HSYA is 1.5 mg/kg, which is lower than the level at which saline is administered. HSYA was able to lessen the amount of damage that glutamate and NaCN did to the neurons.

Mice and rats were used in the research to study the effects of the flower extracts of carthamin and mogami-benibana (Carthamustinctorius). DPPH, singlet oxygen, and superoxide are all examples of reactive oxygen species that can be neutralised by mogami-benibana water. Carthamin, an antioxidant found in saffflower petals, is capable of counteracting the damaging effects of DPPH radicals.

The influence of HSYA on the I/R of the spinal cord was investigated using rabbits. The neuroperformance of HSYA was significantly higher than that of I/R. As a result of the efficacy of HSYA, there was a marked decrease in the number of cases of I/R spine necrosis. HSYA increases the activity of SOD while simultaneously lowering MDA levels. Apoptosis brought on by I/R could not be stopped by HSYA treatment.

The development of lymphostatic encephalopathy can be avoided in rats by administering HSYA to the animals. In order to explore the ANS control, rat ECG HRV was utilised. The laboratory LE rats exhibited signs of improvement after being given an intraperitoneal dose of HSYA (five milligrammes per kilogramme). In the medulla, LE was found to promote apoptosis, which was inhibited by HSYA (RVLM). The cardioautonomic regulation of the LE muscle was improved as a result of HSYA. Both the protein and mRNA levels were decreased by HSYA in the LE RVLM eNOS cell line. The brain is shielded from the

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deleterious effects of LE by HSYA. Ischemic rats benefited from the HSYA treatment. Rats in whom the MCA supply had been cut off exhibited signs of brain ischemia under these conditions. After 30 minutes of ischemia, sublingual injections of 1.5, 3.0, and 6.0 mg/kg of HSYA were given, whereas a control dose of 0.2 mg/kg of nimodipine was provided. The researchers observed and documented evidence of neuropathy and infarcts within the first twenty-four hours of observation. Both the incidence of brain infarctions and the prevalence of neurological impairment fell as a direct result of HSYA. HSYA proved to be a successful treatment for cerebral ischemia, much like nimodipine did. Utilization of HSYA was associated with reductions in thrombus of 20, 36, and 54.2 percent. Platelet aggregation was decreased by HSYA by a factor of 41.8%. TXA2, not PGI2, was the gene that was silenced, contrary to what was previously believed. Because of HSYA, there was an increase in the viscosity of the erythrocytes as well as an increase in their ability to aggregate. There is a dose-dependent relationship between the effects of carthamus on neuronal apoptosis (bcl-2, caspase-3). MCAO for two hours, followed by reperfusion for anywhere between four and twenty-two hours. The volume of the infarct was reduced as a result of the high doses of medicine (P0.05). The high dose of therapy increased bcl-2 while simultaneously lowering caspase-3 (P0.05). The effect that HSYA has on the mtPTP levels of rats in the laboratory. HSYA was able to minimise the increase in mitochondrial size caused by Ca^{2+} and H2O2 in this experiment. The synthesis of ATP and the rate of respiration in the mitochondria were both increased by HSYA. At concentrations ranging from 10 to 80 micromol/l, HSYA was able to lower the amount of mitochondrial Ca^{2+}-ROS.

- ***Cassia occidentalis***

In order to investigate the effects of the floral extracts of carthamin and mogami-benibana, the researchers made use of both mice and rats in their experiments (Carthamustinctorius). The reactive oxygen species DPPH, singlet oxygen, and superoxide can all be neutralised by mogami-benibana water. Other reactive oxygen species include superoxide. The antioxidant known as carthamin, which can be found in the petals of saffflower, is able to neutralise the potentially harmful effects of DPPH radicals.

The effect of HSYA on the I/R of the spinal cord was studied with rabbits as the subjects of the experiment. It was shown that HSYA had neuroperformance that was noticeably superior than that of I/R. The number of instances with I/R spine necrosis dropped significantly as a direct result of the effectiveness of HSYA, which resulted in the reduction. HSYA boosts the activity of superoxide dismutase (SOD) while simultaneously reducing levels of MDA. The treatment with HSYA was not successful in stopping the apoptosis that was caused by I/R.

Through the administration of HSYA to the rats, it is possible to prevent the development of lymphostatic encephalopathy in the animals. Rat ECG HRV was used in this study so that the ANS control could be investigated. After receiving a dose of HSYA intraperitoneally in the laboratory, the LE rats showed symptoms of improvement (five milligrammes per kilogramme). In the medulla, it was discovered that LE promoted apoptosis, but HSYA was able to block this process (RVLM). As a consequence of HSYA, the LE muscle's cardioautonomic control was able to function more normally. In the LE RVLM eNOS cell line, the levels of both protein and mRNA were reduced as a result of treatment with HSYA. Because of HSYA, the harmful effects of LE are prevented from having an influence on the brain. The HSYA therapy was beneficial for the rats that were ischemic. Under these conditions, rats in whom the MCA supply had been cut off exhibited evidence of cerebral ischemia. [Citation needed] After 30 minutes of ischemia, sublingual injections of 1.5, 3.0, and 6.0 mg/kg of HSYA were administered, while a control dose of 0.2 mg/kg of nimodipine was also delivered. Within the first twenty-four hours of their observation, the researchers found evidence of neuropathy as well as infarcts, which they then documented. As a direct consequence of HSYA, the number of cases of brain infarction and the number of people living with neurological impairment both decreased. A similar level of success was seen with the use of HSYA as a therapy for cerebral ischemia as that seen with nimodipine. There was a correlation between the utilisation of HSYA and reductions in thrombus of 20, 36, and 54.2 percent. Platelet aggregation was reduced by a factor of 41.8 percent as a result of HSYA treatment. In contrast to what was previously assumed, the gene that was silenced was TXA2, not PGI2. Because of HSYA, there was an increase in both the viscosity and the ability of the erythrocytes to combine. Both of these changes occurred simultaneously. There is a link between the effects of carthamus on neuronal apoptosis and the dose at which it is administered (bcl-2, caspase-3). MCAO for a period of two hours, followed by reperfusion for a period ranging anywhere from four to twenty-two hours. As a direct result of the high doses of medication, the size of the infarct was significantly decreased (P0.05). The high dose of medication led to a rise in bcl-2 while at the same time leading to a decrease in caspase-3 (P0.05). The effect that HSYA has on the levels of mtPTP in the rats that are being studied in the lab. In this particular experiment, HSYA was successful in reducing the increase in mitochondrial size that was brought on by Ca2+ and H2O2. The use of HSYA led to an increase in both the rate of respiration in the mitochondria as well as the rate at which ATP was synthesised. The amount of mitochondrial Ca2+-ROS was brought down by HSYA when it was present at quantities ranging from 10 to 80 micromol/l.

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In this study, mice and rats were provided with carthamin and Mogami-benibana (Carthamus tinctorius) flower extracts so that the researchers could analyse their effects. In addition, Mogami-benibana water has the ability to reduce the effects of superoxide, DPPH, and singlet oxygen when used in conjunction with water. Carthamin, a chemical found in the petals, has the potential to scavenge some of the radicals that are found in saffron flowers. Rabbits were used in the investigations of the I/R effects of HSYA that were carried out in the laboratory. As an illustration, HSYA possessed greater cognitive ability compared to I/ R. The severity of I/R spine necrosis was lessened as a result of HSYA. Because of the use of HSYA, levels of SOD are increasing while levels of MDA are decreasing. Apoptosis was caused by I/R, but HSYA was able to halt its progression. HSYA has been shown to prevent the development of lymphostatic encephalopathy in rats. The ANS control was evaluated using the rat ECG HRV as the measuring tool. The intraperitoneal injection of HSYA at a dose of 5 mg/kg demonstrated to be beneficial in the treatment of LE rats.

HSYA prevented LE from initiating apoptosis in the test subject's medulla by acting as an inhibitor (RVLM). The cardioautonomic regulation of the LE muscle was improved as a result of HSYA. As a consequence of being treated with HSYA, the levels of eNOS mRNA and protein in the LE RVLM decreased. The brain is shielded against the deleterious effects of LE thanks to HSYA. In rats with ischemia, HSYA therapy showed encouraging signs of improvement. Ischemia of the brain was observed in rats that had an obstruction of the MCA origin. After 30 minutes of ischemia, injections of HSYA at doses of 1.5, 3.0, and 6.0 mg/kg were given sublingually, while nimodipine was given at a dosage of 0.2 mg/kg. After a period of 24 hours, neuropathy and infarcts were identified and recorded for the patient. The HSYA regimen resulted in far less damage being inflicted upon the neurological system. In a manner comparable to that of nimodipine, HSYA was successful in treating patients who had cerebral ischemia. With HSYA, thrombus reductions of 20, 36, and 54.2 percent were attained. Platelet aggregation was decreased by HSYA by a factor of 41.8%. According to the findings of this research, PGI2 was not inhibited, however TXA2 was. The addition of HSYA resulted in an increase in viscosity as well as erythrocyte aggregation. There is a dose-dependent relationship between the effects of carthamus on neuronal apoptosis (bcl-2, caspase-3). Reperfusion could take up to 22 hours to complete, depending on how long the MCAO was in effect. At large doses, there was a decrease in the volume of the infarct (P0.05). Bcl-2 levels increased, however caspase-3 levels decreased as a direct consequence of the high dosage (P0.05). The influence of HSYA on mtPTP activity in rats. The growth of Ca2+ and H2O2 in mitochondria was decreased because to HSYA. The incorporation of HSYA into the medium at concentrations ranging from 10 to 80 micromol/l resulted in an increase in both mitochondrial ATP generation and respiration.

- ***Coriandrum sativum***

The neuroprotective properties of HSYA were shown to be effective in preventing glutamate's induction of neurotoxicity in rat cortical neurons. There was a reduction in the amount of neurodegeneration that occurred as a consequence of the HSYA therapy. It was demonstrated that HSYA was successful in lowering Bax levels while preserving the participants' overall protein balance. Within an environment containing HsYA, there was no evidence of an NMDA-induced overexpression of NR2B. For protection against neurodegenerative conditions, make use of astragali, ligusticum wallichii, angelica sinensis, and carthamus tinctorius. When there is an increase in blood flow to the brain, patients suffering from Alzheimer's disease and Parkinson's disease experience an improvement in their symptoms. hydroxysafflor yellow A possesses neuroprotective properties that are of benefit to the nervous system (HSYA). After administering HSYA to male WKY rats that had been infected with MCAO, the researchers looked for evidence of brain injury in the animals. The infarction symptoms were visible in the slices of brain tissue. HSYA protects embryonic cortical cells from glutamate and cyanide injury (NaCN). The amount of neurological damage and the size of the infarct that was caused by ischemic rats treated with HSYA was reduced when the rats were given dosages of 3.0 and 6.0 mg/kg. Imodipine is 0.02 percent HSYA. The neuroprotective dose of HSYA administered sublingually is 1.5 mg/kg, which is the same as the concentration of sodium chloride found in seawater. It has been demonstrated that the application of HSYA can lessen the amount of damage that is caused to neurons as a result of glutamate and NaCN.

Both mice and rats were used in the research to investigate the effects of Mogami-benibana (Carthamustinctorius) flower extracts as well as carthamin. One of the many outstanding qualities of mogami-benibana water is that it deactivates reactive oxygen species like singlet oxygen and superoxide. This is just one of the water's numerous properties. Carthamin, which can be found in the petals of saffron, has the ability to eliminate DPPH radicals from the surrounding environment.

The effect of HSYA on the I/R activity of the spinal cord was investigated using rabbits. When comparing neuroperformance, HSYA came out on top vs I/R. A study found that the administration of HSYA resulted in a reduction in the severity of I/R spine necrosis. SOD is increased by HSYA, albeit at the expense of MDA. The presence of HSYA was able to inhibit apoptosis caused by I/R

The use of the HSYA medication makes it feasible to protect rats from developing lymphostatic encephalopathy. An electrocardiogram with heart rate

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variability (ECG HRV) was performed on rats in order to investigate how effectively the ANS controls its own heart rate as well as other physiological factors. The condition of the LE rats was significantly enhanced by the intraperitoneal administration of HSYA at a dose of 5 mg/kg.

HSYA was able to prevent the enhanced medulla apoptosis that was caused by LE (RVLM). The cardioautonomic regulation of the LE muscle was improved as a result of HSYA. The quantities of protein and mRNA that are produced by LE RVLM eNOS were successfully reduced by the use of HSYA. The HSYA provides protection for the brain against the deleterious effects of LE. The administration of HSYA to rats suffering from ischaemia was beneficial. Signs of cerebral ischemia were observed in rats in whom the MCA origin had been occluded. In comparison, an injection of 0.02 mg/kg of nimodipine was given 30 minutes after the infarction. Hsya was injected at a rate of 1.5 mg/kg, while the nimodipine dose was 0.02 mg/kg. Following a period of monitoring lasting twenty-four hours, it was determined that neuropathy and infarcts were present. To put it another way, the HSYA method led to a reduction in the number of brain infarcts as well as the amount of damage to neural tissue. Hsya was able to reverse the effects of cerebral infarction in the exact same way that nimodipine could. According to the findings of the study, the utilisation of HSYA resulted in a reduction in thrombus that was 20 percent, 36 percent, and 54.2 percent respectively. The utilisation of HSYA was responsible for a reduction of 41.8% of the platelet aggregation. The inhibition was directed on TXA2, not PGI2, as its target. When HSYA was present, it was seen to increase both the viscosity of the solution and the erythrocyte aggregation. There is a dose-dependent relationship between the effects of carthamus on neuronal apoptosis (bcl-2, caspase-3). A blockage of the middle cerebral artery for two hours, followed by reperfusion for either four or twenty-two hours. The infarct volume was significantly decreased by the high doses (P0.05). The high dosage of the medicine resulted in decreased levels of caspase-3 while simultaneously increasing levels of bcl-2 (P0.05). In order to investigate the effects of HSYA on the levels of mtPTP in rats, the animals were fed the compound. While Ca2+ and H2O2 were able to stimulate mitochondrial growth, HSYA was successful in inhibiting this process. Through the use of HSYA (10-80 micromol/l), it was possible to produce decreased levels of mitochondrial Ca2+-ROS as well as increased levels of ATP and respiration.

- ***Crocus sativus***

HSYA was found to have neuroprotective qualities in the cortical neurons of rats, which protected them from the neurotoxic effects of glutamate. As a result of HSYA, there was a decrease in neurodeath. HSYA was successful in lowering Bax while maintaining a satisfactory protein to carbohydrate ratio. HSYA was successful in preventing NMDA from producing an excessive amount of NR2B. Plants such as astragali, ligusticum wallichii, angelica sinensis, and carthamus tinctorius have been shown to slow or stop the progression of neurodegenerative disease. When there is more blood flowing to the brain, patients suffering from Alzheimer's disease and Parkinson's disease experience an improvement in their symptoms. Neuronal protection afforded by the actions of hydroxysafflor yellow A (HSYA). After giving HSYA to male WKY rats with MCAO, the brain damage of the animals was examined after the administration of the compound. Evidence of infarction could be seen in slices taken from the brain. HSYA protects embryonic cortical cells from glutamate and cyanide injury (NaCN). When HSYA was administered to rats at a dose of 3.0 mg/kg, both the severity of neurological impairment and the size of infarcts were significantly reduced. Imodipine is 0.02 percent HSYA. The neuroprotective dose of sublingual HSYA is 1.5 mg/kg, which is lower than the level at which saline is administered. HSYA was able to lessen the amount of damage that glutamate and NaCN did to the neurons.

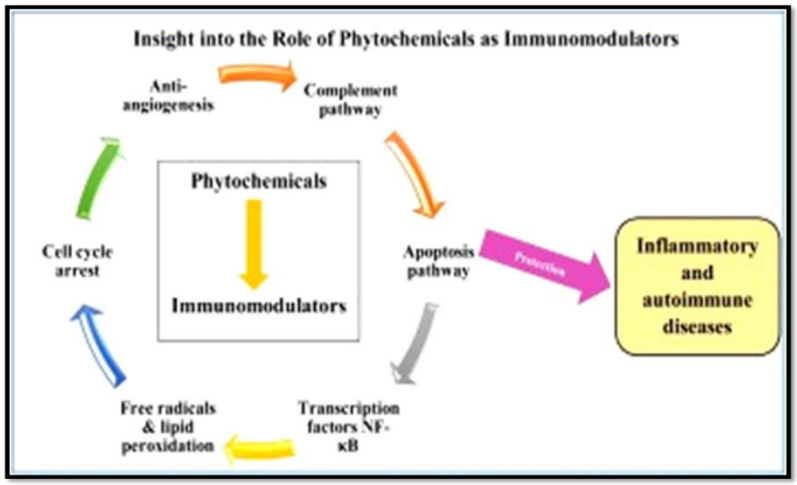

Fig: 1 Shows Antioxidant, Immuno-modulatory Activity of various herbal plants

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- ***Melilotus officinalis***

In rats suffering from brain ischemia, an ethanol extract of chamomile and matricaria was demonstrated to lessen the severity of motor dysfunction. After an injury caused by ischemia and reperfusion, chamomile was discovered to improve motor function. The levels of MDA increase whenever there is ischemia followed by reperfusion. The antioxidant capacity of the brain, as well as the antioxidant capacity of the serum, as well as NO, were unaffected by it. DacriovisTM was developed with the intention of preventing oxidative stress and inflammation in human corneal epithelial cells, both of which can be brought on by prolonged exposure to UVB light. HCEC-12 cells were treated with eyedrops after being subjected to UVB radiation. The researchers investigated the health of the cells, the rate at which wounds healed, and the extent to which proteins and lipids were damaged by oxidation. In addition to this, they investigated how the COX-2, IL-1, and GSS genes were expressed. (Table:1) Eyedrops were able to lower the amount of cell death caused by exposure to UVB light, which led to faster wound healing. There was a discernible decrease in the amount of ROS, protein, and lipid that were damaged by oxidation. As a consequence of this, it inhibited the effect that UVB had on GSS, in addition to HO-1 and SOD-2.

Table: 1 Herbal plants phytochemical affect on Neuro-Disease Treatment

Plant Name	Proposed for treatment	Phyto-chemical Group	Reference
Acorus calamus	Hyperlipdemia	Monoterpene	[52]
Centella asiatica	Dementia, Cerebral	Isothocyanate	[54]
Corydalis ternate	Depression dysthymia	Alkaloid	[53]
Curcuma longa	Congestive and Physical sluggishness	Phenols	[55]
Glycyrrhiza glabra	Anixety, Ischemic	Saponins, Triterpenoid	[59]
Huperzia serrata	Enhancing memory and promote longevity	Alkaloids	[48]
Zinger officinate	Anixety, Ischemic, Hyperlipdemia	Phenols	[45]
Emblica officinalis	Congestive and Physical sluggishness, Anixety, Ischemic, Hyperlipdemia	Vitamin, polyphenols, Alkaloids	[43]

- ***Melissa officinalis***

The study found that administering an extract of the lavender plant known as matricaria chamomilla to rats with brain ischemia resulted in a reduction in the severity of motor dysfunctions. It was discovered that chamomile was able to lessen the effect that I/R had on motor functions. MDA levels are increased both by ischaemia and reperfusion. The medication did not have any effect on the antioxidant capacity of the brain, the serum levels, or the levels of NO. Human corneal epithelial cells treated with DacriovisTM are protected from the oxidative damage and inflammation that are caused by UVB radiation. The HCEC-12 cells that had been exposed to UVB had eyedrops applied to them. In addition to looking at these genes, this study also looked at cell viability, wound healing, and levels of reactive oxygen species (ROS). In addition, the oxidative damage to lipids and each of these other components were investigated in this study. The use of eyedrops in this study allowed both faster wound healing and reduced cell death caused by UVB exposure. The investigation was carried out on rats. There was a lessening of the oxidative damage to the proteins and lipids. Additionally, GSS and SOD-2 were protected from the damaging effects of UVB.

- ***Mentha longifolia***

The reduction of motor dysfunctions in rats with brain ischemia was attributed to an ethanol extract of chamomile and matricaria. Chamomile was able to alleviate some of the motor impairment caused by I/R. Ischemia and reperfusion are both associated with an increase in MDA levels. The antioxidant capacity of the brain, serum, or NO remained the same throughout the experiment. DacriovisTM was developed to shield human corneal epithelial cells from the oxidative damage and inflammation that are caused by exposure to UVB light. When we tested eyedrops on HCEC-12 cells that had been subjected to UVB radiation in the past, we got the best results. We looked into things like cell viability and how effectively wounds heal, as well as ROS levels, oxidative protein and lipid damage, and the expression of genes like COX-2 and IL-1. These are just some of the things that we looked into (table:2). Utilizing eyedrops resulted in a reduction in UVB-induced cell death and an acceleration of wound healing. The oxidative damage to proteins and lipids, as well as ROS, was decreased. In addition to restoring HO-1, it was also able to prevent GSS and SOD-2 from being damaged by the impacts of UVB.

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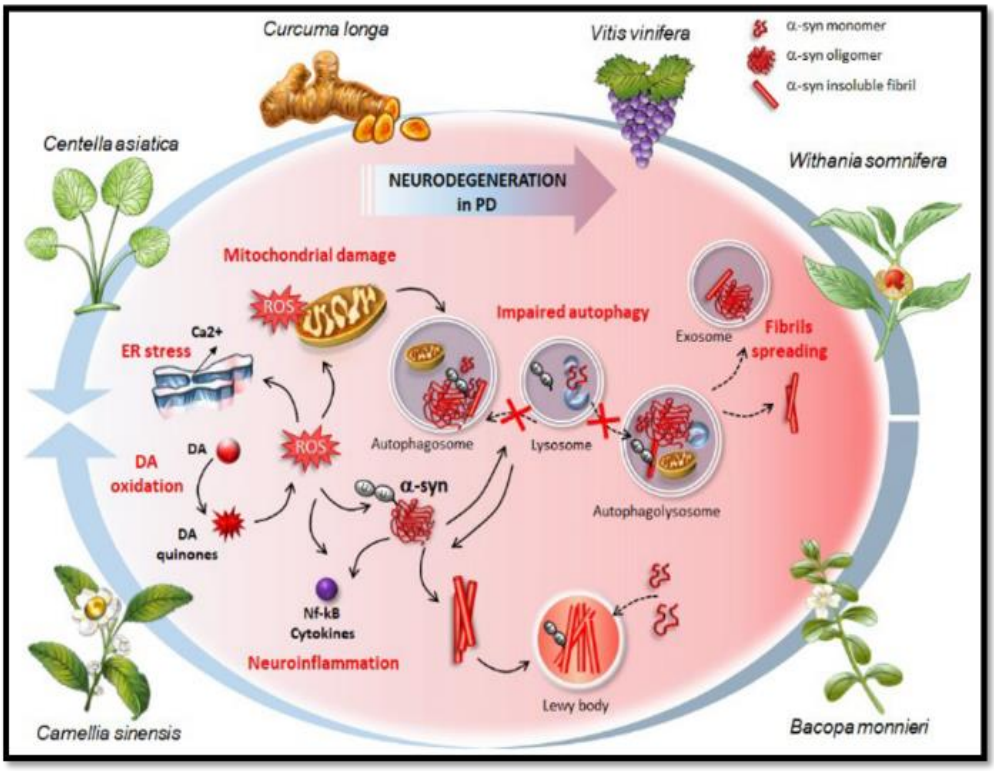

Fig: 2 Herbal plants shows Neuro-protective activity

Table 2: Plant Derivative Shows Therapeutic Activity on Neuro Degenerative Disease

Plant Name	Active Constituents	Phyto-chemical Group	Activity
Acorus calamus	Asarone	Monoterpene	Sedative, Caple to improve memory
Centella asiatica	Asiatic acid, Centelloside	Isothocyanate	Brain tonic, anti-anxiety
Corydalis ternate	Protropne	Alkaloid	Anti-Cholnesterase, anti-amnesic
Curcuma longa	Curcumin	Phenols	Protect against synaptic dysfunction
Glycyrrhiza glabra	Glycyrrhizin	Saponins, Triterpenoid	Improve learning and memory on scopolamine
Huperzia serrata	Huperzine A and B	Alkaloids	Action on neuromuscular systems
Zinger officinate	Zingerone, shogaol	Phenols	Brain acetyl cholnesteras inhibition
Emblica officinalis	Vit.Cphyllembin	Vitamin, polyphenols, Alkaloids	Anti- cholinesterase activity

Phyto-chemical work in Neuro-disease

There is evidence to suggest that phytochemicals found in herbs can lessen the risk of major illnesses such as autoimmune, cardiovascular, and neurological diseases. Curcumin, resveratrol, proanthocyanidins, and ferulic acid are four examples of common polyphenols that have been the subject of a number of research that demonstrate their anti-inflammatory and antioxidant properties. The fact that these phytochemicals have been shown time and again to have neuroprotective qualities provides compelling evidence that they may be able to reduce the signs and symptoms of depression. The antidepressant activities of the phytochemicals are outlined in Table 3.

Phyto-chemical	Dose	Study design	Mechanism of Action
Carvacrol	14.6mg/kg	Oral administration to rats	Induce anti-depressent effects that seem to be dependents on the intraction with the dopamine brain pathways
Curcumin	15-30mg/kg	Intra-peritoneal inj. In mice	Enhance 5-HT level

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Ferulic acid	110-250mg/kg	Oral administration to rats	Attenuate stress-induced behavior Increase CREB phosphorylation and brain-derived neurotropic factor mRNA level in the hippocampus
L-theanine	0.5- 20 mg/kg	Oral administration to rats	Reduce immobility time in the forced swimming test and tail suspension test without ambulation in the open field test.
Proanthocyanidin	24-48 mg/kg	Oral administration to rats	Reduce immobility period in the forced swimming test and tail suspension test Enhance 5-HT levels in hypothalamus, hypothalamus, and frontal cortex
Quercetin	20-40mg/kg	Oral administration to rats	Prevent hyperactivation of the HPA axis

Carvacol: Oregano and thyme are examples of aromatic plants that belong to the Lamiaceae family. These herbs contain a substantial quantity of carvacrol, also known as 2-methyl-5-(1-methylethyl) phenol, which is the predominant natural component found in the essential oil portion of the herb. In order to produce this monoterpenic phenol, the p-cymene found in -terpinene must first be transformed to methyl and isopropyl on the para position of the phenol ring.

The Food and Drug Administration (FDA) has given their approval for carvacrol to be used in food, and the Council of Europe has included it on their list of authorised chemical flavourings. The presence of carvacrol in oregano was thought to have a direct influence on the biological activity of the plant; this was one of the hypotheses that was tested. Traditional medicine has made use of carvacrol-based medications and essential oils for a number of centuries, and there are currently a great deal of carvacrol-based feed additives accessible on the market. Natural therapies were found to be more popular with the general public than pharmaceuticals when it came to increasing focus, mood, and memory, as the result of an experiment that researched the attitudes of general practitioners and the public toward medicines and natural treatments for increasing focus, mood, and memory. Even though additional research on the mechanism of action is required, it is common practise to employ plant-derived metabolites like carvacrol in healthy people in order to improve both their mood and their cognitive abilities.

According to the findings of a number of different research, carvacrol possesses qualities that make it effective against fungi, insects, and bacteria. Carvacrol has been discovered to have "strong antimutagenic activities" in addition to its anticancer and anticarcinogenic capabilities in vitro. It has been demonstrated that this phytochemical can protect the livers of rats from the ischemia/reperfusion (I/R) injury. This volatile molecule is able to easily pass through membranes such as the blood-brain barrier because of the lipophilicity that it possesses. Once within the brain, it interacts with a number of receptor sites in the central nervous system (CNS). To this day, there have only been a few of studies conducted to examine its effects on the CNS in vivo. Researchers working with HEK cells and primary grown cells from the CA3–CA1 region of the hippocampus found that carvacrol inhibits the activity of the TRP Cation channel subfamily M, member 7 (TRPM7). It has been demonstrated that TRPM7 is an essential component in the degeneration of neurons caused by a lack of oxygen. Therefore, the hypothesis states that inhibiting TRPM7 will reduce the amount of cell death that occurs as a result of ischemia and brain injury. Recent research has shown that carvacrol can reduce the risk of sustaining an I/R injury to the brain. Because the hydroxyl group of carvacrol binds to AChE, it suppresses the activity of the enzyme and has the potential to be beneficial in the treatment of neurodegenerative illnesses such as Alzheimer's disease and Parkinson's disease. According to the most recent research, tests conducted on rats suffering from anxiety and depression revealed that carvacrol exhibited features of both an anxiolytic and an antidepressant. The bioactivity of this particular molecule, which has the potential to influence both mood and cognitive processes, most likely involves participation from multiple neurotransmitter systems within the brain.

Curcumin: Major depression is characterised by a persistently sad mood, an absence of interest in previously enjoyable activities, a loss of weight or an increase in weight, disturbances in sleep (including insomnia and hypersomnia), agitation or retardation of

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motor function, exhaustion or a lack of energy, and an increased desire to end one's own life. When a new outbreak occurs, around 15–20 percent of the world's population is impacted by it. Even though antidepressants are easily available, we are still unable to treat anywhere from 20 to 30 percent of the people who suffer from depression. Antidepressants are associated with a lengthy number of adverse effects as well as interactions with a variety of substances, including meals, beverages, and other medications. As a result, there is an urgent need to discover new pharmacological treatments that are not only effective but also secure for the treatment of severe depression. Curcumin has been found in a number of experiments conducted on animals to possess antidepressant qualities. Curcumin demonstrated an antiimmobility effect when administered intravenously at doses ranging from 10 to 80 mg/kg. The test lasted for six minutes. Following treatment for ninety minutes, the anti-immobility effect reached its maximum level. Curcumin, when administered in doses of 40 and 80 mg/kg, was able to reverse the behavioural depression brought on by reserpine in mice. Since then, it has been discovered through additional research that curcumin boosts the anti-immobility activity of the MAO inhibitors tranylcypromine (5 mg/kg, intravenously) and selegiline (5 mg/kg, intravenously). Both of these treatments are administered intravenously. According to the findings of this study, the antidepressant qualities of curcumin may be related to the enzyme known as monoamine oxidase. According to research that was conducted in the past, curcumin is able to inhibit the activity of both the MAO-A and the MAO-B enzymes. It's important to point out that monoamine oxidase is the enzyme that breaks down norepinephrine, serotonin, and dopamine, so keep that in mind. Curcumin, which inhibits the MAO enzyme, causes the neurotransmitter action to last for a longer period of time by raising its concentration at the synapse.

Ferulic acid: Ferulic acid, which is also known as 4-hydroxy-3-methoxycinnamic acid, is found in a wide variety of plants, the majority of which are flowering plants (FA). In 1866, it was first isolated from the plant Ferula foetida, from which it derives its name. The year also marks the year of its initial isolation. Cereal grains have FA concentrations that average 2 grammes per kilogramme of their dry weight. The plant's fatty acid (FA) metabolism starts off with aromatic amino acids and then moves on to the shikimate pathway as the first step. When phenylalanine or tyrosine is employed in the synthesis of p-coumaric acid, the caffeic acid that is produced as a byproduct is then subjected to a methylation process in order to produce FA. Lignin is a type of polymer that is formed from fatty acid chains, arabinoxylans, and hemicelluloses. Lignin is what gives the cell wall its rigidity. It is possible to find it in its free form, dimerized form, or esterified with proteins and polysaccharides in a wide range of natural goods. In the process of germination, FA shields plant cells from damage caused by hydrolytic enzymes, regulates plant growth, prevents the growth of competing plants, and absorbs minerals and water from the roots. Because FA is present, cereal crops can also be protected from fungal illnesses and insect infestations.

L-Theanine: Theanine, also known as N-ethyl-L-glutamine, is among the most beneficial of the amino acids that can be found in green tea. Since it was discovered that L-theanine can act as a relaxing agent, scientists have been conducting research into its pharmacology. Studies on animals' neurochemistry have shown, for instance, that L-theanine has a micromolar affinity for NMDA and AMPA receptors, and that it also increases the levels of serotonin, dopamine, and GABA in the brain. The neuroprotective effects that this chemical demonstrates in animal models might be attributable, in part, to the fact that it exerts antagonising effects on group 1 metabotrophic glutamate receptors. Research conducted on animals demonstrates that both learning and memory can be enhanced. According to the neuropharmacology of L-theanine, additional research in animals and humans is required to identify whether or not it has qualities that are neuroprotective and cognitive-enhancing.

III. CONCLUSION

There are several drugs, which have been used for NDDs till date, but they do not possess the efficacy to amend the disease progression, rather they exert copious side effects. Frequent disease amending strategies have been discovered in the recent years and numerous compounds are being explored under these strategies but none of them have successfully grasped the market. In this perspective, plant grounded drugs have also developed as an innovative acumen. Numerous natural alkaloids retain mounting effects in the treatment of several NDDs. Along with modulating neurotransmitter system, natural alkaloids also possess anti-amyloid, anti-inflammatory, and antioxidant properties as well as anti-depressive and anti-convulsing efficacy. Thus, natural alkaloids possess multiple mechanistic approaches in the treatment of NDDs. Alkaloids exert vast neuroprotective actions, but studies are needed on their toxic effects. There are few alkaloids which have been published with their toxic effects. Although many of the alkaloids with their adverse effects need to be reported. It has been suggested that the selection of natural alkaloids in the treatment of NDDs is safe as compared to synthetic drug. Numerous alkaloids and their derivatives have marvelous scope in the treatment of NDDs. But only few of them have prevalent clinical use. There is a vital requirement to design clinical trials for such compounds that are not even entered in the clinical trials till date, because the natural alkaloids are encouraging hope in slowing the development and progression of NDDs.

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