

A review on treatment of Multiple Sclerosis with natural products

A dissertation submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University in the fulfillment of the requirements for the degree of Bachelor of Pharmacy (B. Pharm.)



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Faculty of Allied Health Science

Daffodil International University

APPROVAL

This project, **A review on treatment of Multiple Sclerosis with natural products** submitted to the Department of Pharmacy, Faculty of Allied Health Science, Daffodil International University has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

BOARD OF EXAMINER

Professor Dr. Muniruddin Ahmed
Head of the department
Department of Pharmacy
Faculty of Allied Health Science
Daffodil International University

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Internal Examiner 1

.....

Internal Examiner 2

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Supervised By



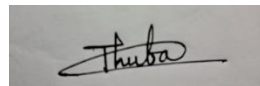
Farhana Israt Jahan

Associate Professor

Department of pharmacy

Daffodil International University

Submitted By



Gazi Kaifera Thufa

Daffodil International University

DECLARATION

I hereby declare that this project report, **A review on treatment of Multiple Sclerosis with natural products** is done by me under the supervision of Farhana Israt Jahan, Associate Professor Department of pharmacy, Faculty of Allied Health Science, Daffodil International University. I am declaring that this project is my original work. I also declare that neither this project nor any thereof has been submitted elsewhere for the award of Bachelor or any degree.

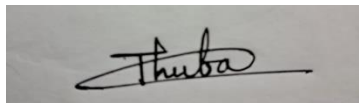
Supervised By



.....

Farhana Israt Jahan
Associate Professor
Department of pharmacy
Faculty of Allied Health Science
Daffodil International University

Submitted By



.....

Gazi Kaifeara Thufa
Department of pharmacy
Faculty of Allied Health Science
Daffodil International University

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DEDICATION

I dedicate this work to almighty Allah ,my parents,instructors and friends

Abstract:

An autoimmune neurodegenerative condition called multiple sclerosis is often brought on by demyelination, axonal damage, and inflammation. Demyelination and, eventually, cognitive impairment are brought on by inflammation of the central nervous system. The use of natural remedies for sickness prevention, treatment, and a decrease in the side effects of pharmaceuticals has increased significantly during the past 10 years. Multiple sclerosis, one of the most common debilitating illnesses in young people, is associated with the deterioration of the myelin sheaths of neurons. Natural remedies not only reduce clinical symptoms but also have the special ability to preserve and heal the neurological system. To evaluate the possible therapeutic advantages of these products in both animals and people, several research have been carried out. An overview of the natural substances that have been shown to be useful in treating MS in both fundamental and clinical trials is provided in this chapter. Natural remedies not only reduce clinical symptoms but also have the special ability to preserve and heal the neurological system. We provide here a systematic review of research that have been published on the topic of treating multiple sclerosis with natural products in order to provide comprehensive information on the use of natural products in the treatment of multiple sclerosis.

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Chapter-1

1.Introduction:

The non-traumatic disabling condition known as multiple sclerosis (MS) most often affects young people . The incidence and prevalence of MS are increasing both in industrialized and developing countries , despite the fact that its fundamental cause is still unclear. MS is a complex condition with several genes that can affect disease susceptibility, in addition to many well-known environmental factors such vitamin D or ultraviolet B light (UVB) exposure, Epstein-Barr virus (EBV) infection, obesity, and smoking [1].

Historically, multiple sclerosis has been referred to as a T-cell mediated organ-specific autoimmune disorder. The prevalent thinking of T-cell autoimmunity, however, is called into question by the efficacy of B-cell-targeted therapies. According to conventional wisdom, MS is a two-stage disease, with early inflammation leading to relapsing-remitting sickness and later neurodegeneration causing non-relapsing progression, including secondary and main progressive MS [2,3]

More extensive immune reconstitution treatment may be able to cure a small number of MS patients and send some of them into long-term remission. More advanced MS patients are hopeful that new promising research on disease-modifying drugs may slow the disease's development while maintaining residual function. The discovery that medicines seem to be successful at different stages of the illness cycle is a serious challenge to the traditional two-stage theory of the natural history of MS[4].

1.1.Etiology:

Demyelination, a chronic condition of the central nervous system (CNS), which is characterized by intermittent and recurrent episodes of inflammation [5]. According to recent studies, MS is thought to be an autoimmune condition where the immune system improperly targets CNS axons by activating T cells that attack the myelin sheath. A lipid-based layer called the myelin sheath helps electrical impulses go back and forth between the spinal cord, which connects the brain to the rest of the body, to the rest of the body. When the myelin is compromised or destroyed, these electrical impulses cannot be transported effectively. Deteriorating myelin areas are replaced by rigid scar tissue. The plaques or lesions that develop as a result further restrict the flow of nerve impulses. The resultant delay in information transmission has the potential to interfere with almost all bodily, sensory, mental, and emotional processes. Even though the specific cause of MS is unknown, both genetic and environmental factors appear to affect a person's likelihood of developing the disease. A recent research [6,7] found that there is a 0.1% probability that MS will develop in the general population. While second- and third-degree relatives (grandparents, grandkids, aunts, uncles, nephews, nieces, and cousins) are at around a 1% risk, a child with one parent with MS is at about a 2% risk. However, it seems that the genetic component of MS risk and environmental factors interact in a complex manner. Smoking, Epstein-Barr virus infection, UV radiation exposure, vitamin D status, and other environmental risk factors have all received a lot of evidence to support them. Epidemiological studies have shown that MS is more common in regions with higher populations of people with northern European ancestry. MS is substantially less common in Asia and tropical and subtropical regions. Interesting to notice is that moving from one place to another appears to alter your risk of developing MS. According to research, immigrants and their children frequently pick up the risk profile of the area they

transfer to. However, it appears that the age of the mover plays a role in this process, as people who move when they are young tend to adapt to the danger level of the new location, but people who move later in life might not notice the change in risk level until the next generation. These findings are consistent with the idea that early exposure to an environmental trigger increases the incidence of MS in a genetically sensitive population[8].

1.2.Pathogenesis:

Pathogen-associated molecules bind to toll-like receptors on APCs, specific cytokines, such as interleukin (IL)-12, IL-23, and IL-4, start to be produced. These cytokines subsequently trigger the differentiation, which can secrete certain cytokines. Both innate and adaptive immunity depend on proinflammatory cytokines including tumor necrosis factor-alpha (TNF-alpha) and interferon gamma (IFN). These cytokines are produced by Th1 cells [9]. They are able to make inflammation worse by blocking Th2 differentiation. Th2 cells generate two anti-inflammatory cytokines, IL-4 and IL-13. IL-4 reduces pathological inflammation by activating alternative M1 macrophages that encourage inflammation and by raising M2 macrophages, also referred to as repair macrophages. IL-13 affects immune cells in a manner similar to that of IL-4. This cytokine has anti-inflammatory properties, especially when allergic inflammation is present. It is generated by the enzyme matrix metalloproteinase. Th17 is a distinct subset of CD4+ T cells that secretes numerous pro-inflammatory cytokines. Multiple sclerosis's development was aided by immune cells and their cytokines. (MS).

B cells and their cytokines have an impact on the pathophysiology of MS as well. These cells can also generate the anti-inflammatory cytokine IL-10. B lymphocytes can therefore influence the emergence of MS in a positive or negative way [10].

Along with the cells mentioned above, numerous studies have shown that CD8+ T cells, also referred to as cytotoxic T cells, can be found in MS lesions. These cells produce cytolytic proteins. Additionally, by increasing vascular permeability, glial cell death, and oligodendrocyte death, these cells have a significant impact on the pathophysiology of MS. The oligodendrocyte death-related myelin repair pathway is also hampered in addition to CNS inflammation. The Fas ligand (FasL) is produced by lymphocyte cells. This ligand causes the death of oligodendrocyte cells, which are TNF receptor superfamily cell surface receptors [11]. As a result, there are less myelin synthesis cells, which has an impact on how the myelin sheath is made.

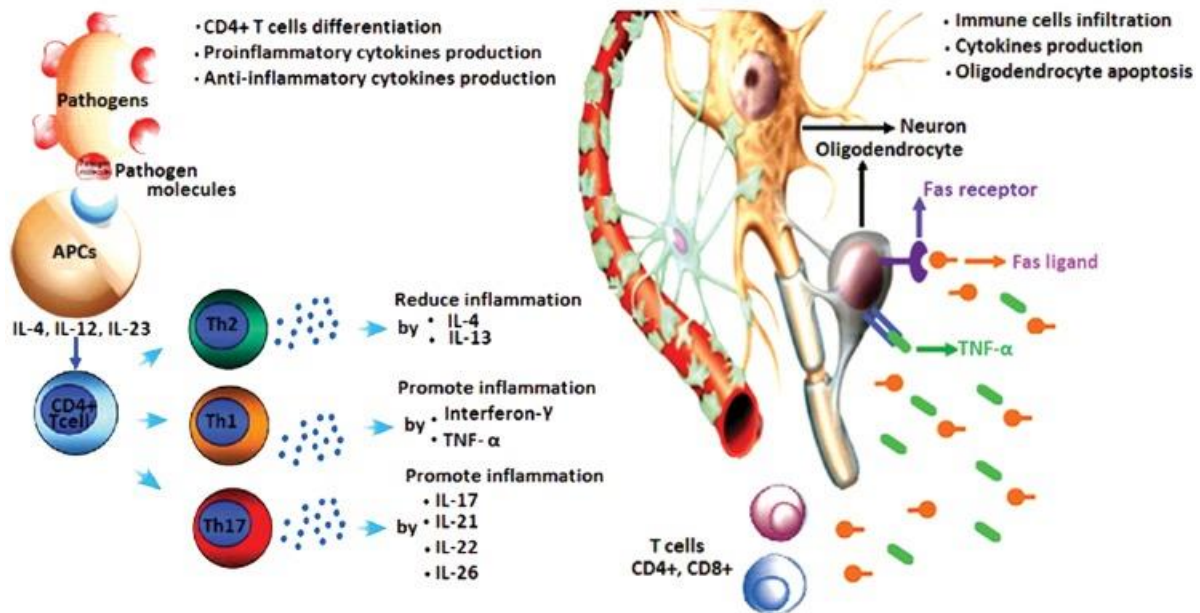


Figure.1.Pathogenesis of multiple sclerosis[12]

1.3.Symptoms:

1.3.1.Fatigue :

The most pervasive and disabling symptom of MS is fatigue. Most MS patients report feeling worn out. There are five different forms of fatigue that MS patients frequently experience. The term "tiredness" can be used to indicate general .

After a demanding, challenging day at work or play, a person with MS is not immune to fatigue. Sometimes it is not acknowledged that having MS does not protect one from feeling this kind of fatigue. We instruct that weariness is a good state since MS patients are not weak and do not break because they have worked hard. In MS, the phrase "rest, rest, rest" is frequently used. The wisest course of action is clearly not to push oneself to the point of exhaustion to see how far one can go before breaking, but someone with MS may absolutely become tired from time to time and recover and work well after a break. Deconditioning weariness is another word for tiredness.

People who lack adequate physical fitness, whether or not they have MS, feel worn out. Building endurance requires aerobic activity. Trying to complete an uncommon task makes you exhausted if you lack endurance. There are two types of tiredness: neuromuscular fatigue and short-circuiting fatigue.

The demyelinated nerve fires continually when given a repetitive task until it shorts. In other words, progressive resistance exercises like weightlifting typically make you feel more weary and weak, as opposed to making you feel stronger. By taking little breaks and conserving energy, you might be able to hide your exhaustion. Depression fatigue is another name for this sort of exhaustion.

People who are depressed frequently struggle with their sleep, eating, and general health, whether or not they have MS. They could call it fatigue, but the goal of treatment is to manage depression.

The most common type of fatigue is seen in 85% to 90% of MS patients. It is frequently referred to as laziness or MS-related exhaustion. For those who haven't done anything and aren't depressed, it manifests as a severe case of exhaustion. Its medication-assisted management has had some degree of effectiveness thanks to neurochemistry. Several medications have shown promise in easing this frequent MS problem, including amantidine, pemoline, methylphenidate, fluoxetine, and now, most frequently, modafinil .

The weariness may be treated using a mix of physical and pharmaceutical methods when those difficulties have been resolved and any concurrent medical conditions that may be contributing (such as heart disease, sleep disorders, or bladder infections) have been treated. [13]

1.3.2.Pain:

Pain is unexpectedly common in MS patients, occurring in 50% of them [14]. Most frequently, the pain is of the burning neuropathic sort. Painkillers have a limited or nonexistent effect on pain, which could be uncomfortable. It's possible that the pain won't have a recognizable neurologic pattern. While it might be paroxysmal in nature, it is typically rather continuous and gets worse at night when the body is sleeping. Antidepressant and antiepileptic medications are typically effective in treating the unpleasant symptoms

1.3.3.The bladder:

MS patients typically struggle with bladder issues. Urgency, hesitation, frequency, and incontinence are a few possible bladder symptoms. The smallest, least functional bladder is the most common. Uncontrolled contractions as well as several of the symptoms mentioned above are frequent. Despite appearing to be visually and biologically different, a large, failure-to-empty bladder overfills and exhibits the same symptoms. A dysynergia between the bladder and the urinary sphincter frequently occurs, which causes a different mechanism to produce the same symptoms. Recurrent bladder infections make the symptoms more difficult and significantly increase the problems. Low postvoid residual is a feature of tiny, failure-to-store bladders. By using ultrasonography or a catheter, this may be measured [15].

1.3.4. Sexual expression :

MS sufferers may need to be extra cautious when engaging in sexual activity. Relationships must still be stressed as being of the utmost importance without diminishing the relevance of true sexual performance in the face of disability. Males are commonly affected by erectile dysfunction. A woman's capacity to express herself sexually may be restricted by vaginal dryness or a diminished or altered sensation in the vaginal area. The advantages of water-soluble vaginal lubricants are widespread in pharmacies. Increased stimulation, vibration, or mild chilling by rubbing a chilled object (like a frozen bag of peas) into the vaginal area can achieve the desired outcome of overcoming the diminished feeling [16].

1.3.5. Depression:

Depression is one of the primary signs of MS and is brought on by changes to the brain's chemistry and structure[17]. It is undeniable that many MS patients also experience chemical (endogenous) depression because of the brain disorder linked to the condition. Reactive (exogenous) depression is common in MS and can be treated with counseling and other non-pharmacological approaches. In comparison to many other neurologic conditions, some of which are regarded to have a worse prognosis, MS appears to have a greater suicide rate .

1.3.6. Cognition:

Amazingly, despite the fact that 50% of MS patients had cognitive impairments, it was long believed that MS did not induce these conditions .10% of adults have substantial problems with memory, planning, thinking, and judgment, which can make daily functioning challenging. Given how frequently the brain transfers information via myelinated channels, it should not be surprising that the problem is widespread. Areas of impairment can be found and highlighted via a neuropsychological assessment. Speech pathologists and occupational therapists can also be useful in pinpointing specific problems and developing solutions. They may be as simple as socializing exercises or they may involve repeated tasking to try to overcome the anatomical issues in the brain. Although they haven't been particularly successful, treatments for Alzheimer's disease patients who have MS subcortical type dementia occasionally work. It is crucial to regularly check patients with impaired cognition for cognitive difficulties since medications taken for other symptoms like tiredness and disorientation may also cause them. Depression may be treated and may be a contributing cause if it is identified.[18]

Table 1. Use of herbal medicines in Multiple sclerosis, according to the symptomatic problem[19]

Usage	Plant
Antidepressant	<i>Hypericum perforatum</i> <i>Crocus sativus</i>
Sleeping problem	<i>Piper methysticum</i> <i>Valeriana officinalis</i>
Improvement in cognitive impairment	<i>Ginkgo biloba</i>
Urinary system dysfunction	<i>Cannabis sativa</i>
Fatigue	<i>Ginkgo biloba</i> <i>Panax ginseng</i>
Anti-inflammatory and neuroprotective	<i>Ginkgo biloba</i> <i>Zingiber officinale</i> <i>Curcuma longa</i>



Chapter-2

2. Purpose of the study:

- The purpose of the study was to determine the effects of various natural products in treatment of multiple sclerosis.
- To find out natural products which have therapeutic efficacy for the management of multiple sclerosis
- To know about the source of natural products
- To know about the symptoms of multiple sclerosis
- Raising awareness about multiple sclerosis



Chapter-3

3.Methodology:

- The English literature that has been published in the previous twelve years is reviewed in this essay, this project work is based on review articles.
- Data for this study was gathered from google scholar, research gate, PubMed, and science direct.
- This current study was prepared by reviewing many published papers.
- The study was conducted for three months
- All collected information in this study was taken from published papers between the years 2000-2022.
- Data was collected and analyzed from review articles



Chapter-4

4.Result

4.1.Herbal therapy in multiple sclerosis:

4.1.1.*Ginkgo biloba*:

A member of the Ginkgoaceae family .Even though they were first discovered in China and Korea, ginkgo trees can now be found everywhere. A leaf extract from *Ginkgo biloba* trees has been used for many years as a treatment to enhance mental clarity and memory. A groundbreaking study that revealed *G. biloba* is a successful treatment for cognitive issues led to the herb's present position. [20] Studies have revealed that ginkgo extract (EGB761), which has anti-inflammatory and platelet-activating factor (PAF)-inhibitory effects, is useful in treating MS. Ginkgolides, the primary component of *G. biloba*, are indicative of the herb's potential therapeutic benefit for MS through its influence on PAF activity.It is now known that ginkgo can inhibit this process due to the introduction of PAF's relevance in the inflammatory process.[21] *Ginkgo* also reduces fatigue and slows cognitive deterioration in MS patients. Despite the fact that *G. biloba* is generally safe and doesn't have any side effects or negative effects, there have been a few reports of ocular bleeding, headaches, and dizziness associated with its usage.



Figure.2. *Ginkgo biloba* L[22]

4.1.2. *Zingiber officinale*:

An fragrant plant belonging to the Zingiberaceae family. *Z. officinale* is an Indian native that is widely cultivated in Asia, tropical Africa, and Latin America. A common traditional drug and flavorful spice is ginger root. Recent studies have validated ginger's anti-cancer, anti-inflammatory, and antioxidant properties. Because ginger has anti-inflammatory properties, MS patients often consume it. The main gingerols and their dehydrated derivatives (shogaols) that have anti-inflammatory activities are gingerols.[23] 10-gingerols lessen the production of pro-inflammatory cytokines and NO that are brought on by LPS by blocking NF- κ B activation. animal models of multiple sclerosis, ginger's active ingredients (6-shogaol and 10-gingerol) have been shown to have anti-inflammatory and neuroprotective activities. However, clinical studies on MS patients are still needed to confirm these results.



Figure.3. *Zingiber officinale*[24]

4.1.3. *Curcuma longa*:

Southeast and southern tropical Asia are home to the tropical plant *Curcuma longa* L. *C. longa* belongs to the Zingiberaceae subfamily of ginger plants. The yellow color of *Curcuma longa*'s roots is caused by a compound called curcumin. Curcumin, a spice and pigment with nutritional value, is commonly used. It is widely used to treat biliary issues, anorexia, cough, sinusitis, and sore throats in traditional Asian medicine. Numerous biological effects of curcumin have been demonstrated in studies, including anti-inflammatory, anti-cancer, and antioxidant effects. Evidently, several research have looked into curcumin's anti-inflammatory effects.[25,26] The two primary mechanisms by which curcumin reduces inflammation are inhibition of pro-inflammatory cytokines and inhibition of Th17 formation and related pathways.



Figure.4. *Curcuma longa*[27]

4.1.4. *Hypericum perforatum* :

A flowering plant belonging to the Hypericaceae family. It is Originally from Europe and Asia, has now spread to other parts of the world. It is a well-liked plant because of its many medicinal benefits for conditions like anxiety, sadness, and menstruation problems. Currently, *H. perforatum* is utilized to treat problems associated with inflammation, malignancies, and neurological diseases. [28] According to studies, hypericin a key component has a strong affinity for the dopamine-regulating Sigma receptors and has a significant inhibitory impact on the MAO enzymes. Numerous studies concentrate on Hyperforin, another component of this plant that is thought to have medicinal value. It is effective in treating depressive symptoms. MS sufferers may benefit from *H. perforatum*'s antidepressant, antioxidant, and anti-inflammatory effects.

4.1.5. *Valeriana officinalis*:

The valerian plant, *Valeriana officinalis* L., is indigenous to regions of Asia, Europe, and North America. A member of the Caprifoliaceae plant family, and both its root and rhizome have a variety of therapeutic uses. Valerian was used as a medicine in ancient Greece for a variety of ailments, including urinary tract infections, epilepsy, and stomach issues. Valerian was also made available as a therapy for insomnia and sleep issues. The primary contributor to tiredness in MS patients is sleep disruption. [29] Valerenic acid, a key component of root extract, has been shown in clinical studies to be useful in treating mild to severe sleeping disturbances. Patients receiving therapy with valerenic acids have occasionally had side effects such as nausea and allergic response.



Figure.5. *Valeriana officinalis*[30]

4.1.6. *Nigella sativa*:

Belongs to Ranunculaceae family..Many studies have shown that it has medicinal advantages.[31,32]Thymoquinone, the primary compound in *N. sativa* oil, has been demonstrated in in vitro studies to have an inhibitory effect on the production of inflammatory mediators such IL-1b, IL-6, TNF-a, IFN-c, and PGE2. Additionally , it also successfully inhibits non-enzymatic peroxidation in brain phospholipid liposomes.*N. sativa* has demonstrated therapeutic effects in MS animal models.

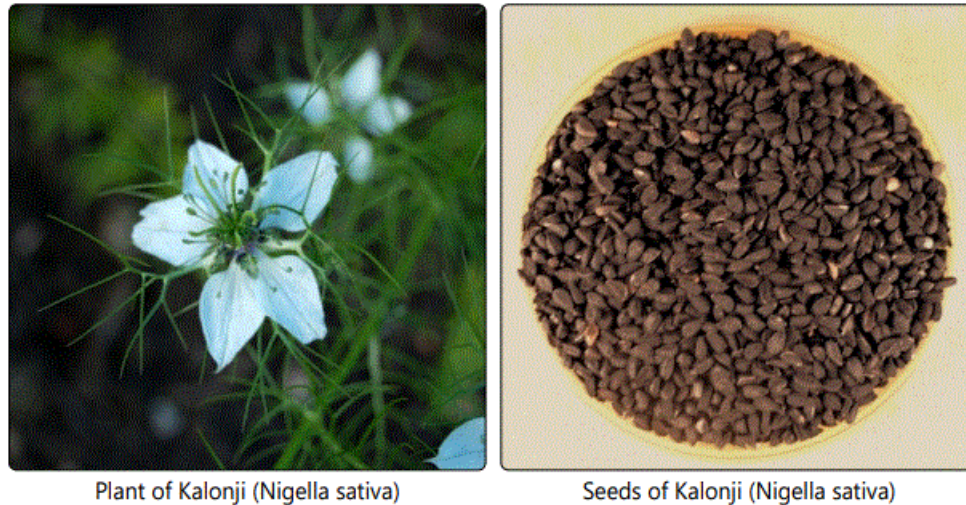


Figure.6.*Nigella sativa*[33]

4.1.7.Crocus sativus:

Saffron a flowering plant of the Iridaceae family. A common medicinal herb for treating a number of ailments is the stigma of the saffron plant..According to several research , saffron may be helpful in the treatment of hypertension and memory issues. Studies revealed that it has anti-inflammatory effects.Crocetin and crocin, the two main active ingredients in saffron stigma .[34-35] In MS lesions, Syncytin-1 expression has been found to be higher in microglia, astrocytes, and glial cells. According to research, crocin has antidepressant qualities for mild to moderate depression. When taken excessively, saffron can induce nausea, vomiting, diarrhea, and lightheadedness.Depression is a common symptom among MS patients, this reasoning suggests that saffron's antidepressant effects may be highly helpful for MS patients who have depressive disorders.



Figure.7. *Crocus sativus*[36]

4.1.8. *Panax ginseng* :

The Araliaceae family's *Panax ginseng*, sometimes referred to as Asian ginseng .The principal active ingredient in *P. ginseng*, ginsenosides, has anti-inflammatory properties. Ginseng may help MS patients by lowering inflammation and fatigue, according to some research.[37] This suggests that ginseng is a helpful medication for reducing fatigue brought on by MS and raising patients' quality of life.

4.1.9. *Vitis vinifera* :

It is one of the most significant fruit crops in the Vitaceae family may be found in much of Western Asia, Northern Africa, and Europe..Resveratrol a phenolic compound has been shown to provide a wide range of pharmacological advantages.Numerous studies have shown that resveratrol has anti-inflammatory and neuroprotective properties. [38]it exhibits neuroprotective advantages by preventing microglia activation and lowering the production of proinflammatory

chemicals. Given that resveratrol may cross the blood-brain barrier (BBB), it would be a fantastic alternative for treating neuroinflammatory and neurodegenerative diseases. It has been demonstrated to have neuroprotective effects in a number of neurodegenerative diseases, but further in-depth study on MS is necessary to determine its potential therapeutic advantages.

4.1.10. *Gastrodia elata*:

An herb from the Orchidaceae family known as tianma is a traditional Chinese plant *G. elata* might be viewed as a prospective option for MS treatment due to its neuroprotective and anti-neuroinflammatory properties. It lowers oxygen free radicals and guards against neural deterioration.[39] The GABA-ergic neuronal system allowed *G. elata* to exhibit effects akin to sedatives. Apoptosis, nitric oxide synthase activity, and global ischemia are all things that *G. elata* is said to guard against. Gastrodin is the main compound that has the neuroprotective effects. Vanillin and benzyl alcohol, two more of active ingredients, exhibit anti-inflammatory effects by lowering the formation of reactive oxygen species (ROS) and inhibiting the activity of the cyclooxygenase-1 and cyclooxygenase-2 enzymes. *G. elata* may be an effective therapy for MS patients due to its important protective role in neurorestorative processes.

4.1.11. *Camellia sinensis* :

One of the oldest drinks in existence and a member of the Theaceae family is green tea has several benefits, including the ability to lower body weight, reduce inflammation, and have neuroprotective qualities. One of green tea's most important active compounds, epigallocatechin-3-gallate (EGCG), is thought to be responsible for the plant's anti-inflammatory and neuroprotective properties. [40] The polyphenol EGCG provides a more effective kind of

neuroprotection for the nervous system by lowering inflammatory mediator production, provides protection against inflammation-related harm to dopaminergic neurons by reducing LPS-induced microglial activation. Green tea's anti-inflammatory qualities aid to protect the CNS against neurodegenerative diseases like MS. Green tea also regulates the body's energy expenditure, which may alleviate the fatigue associated with MS.

Table 2. Comparative study of all plants

Plant name	Indication	Compound name	Mechanism
<i>Ginkgo biloba</i>	Fatigue,Improvement in cognitive impairment,Anti- inflammatory and neuroprotective	Ginkgolides	It effects on the PAF activity
<i>Zingiber officinale</i>	Anti-inflammatory ,neuroprotective	shogaols	1.preventing the depletion of dopamine and reducing the rate of cell death in the central nervous system, suppresses the synthesis of cyclooxygenase-2 (COX-2) and inducible nitric oxide

			synthase (iNOS) in macrophages.
<i>Curcuma longa</i>	Anti-inflammatory and neuroprotective		1.suppression of cytokines that cause inflammation 2.suppression of the pathways involved in Th17 differentiation
<i>Hypericum perforatum</i>	Antidepressant	Hypericin	1.The MAO enzymes are severely inhibited by hypericin, which also has a high affinity for the dopamine-regulating Sigma receptors.
<i>Valeriana officinalis</i>	Sleeping problem	valerenic acid	1.valerenic acid has particular affinity for the GABA A receptor
<i>Nigella sativa</i>	Anti-inflammatory and neuroprotective	Thymoquinone	1.synthesis of inflammatory mediators
<i>Crocus sativus</i>	Antidepressant, Anti-	Crocetin and crocin	1.Blocks syncytin-1

	inflammatory and neuroprotective		and nitric oxide(NO) properties.
<i>Panax ginseng</i>		ginsenosides	1Inflammatory cytokine production, T cell proliferation, and CD25+ cell depletion are all inhibited.
<i>Vitis vinifera</i>	Anti-inflammatory and neuroprotective	Resveratrol	1.reducing the synthesis of proinflammatory molecules and preventing microglia from activating
<i>Gastrodia elata</i>	Anti-inflammatory and neuroprotective	Gastrodin	1.Reduce inflammation by preventing the production of reactive oxygen species (ROS) and cyclooxygenase-(COX-) 1 and COX-2 activity.
<i>Camellia sinensis</i>	Anti-inflammatory	EGCG	1.Reduces the

	and neuroprotective		generation of inflammatory mediators including
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4.2.The Role of Natural Products in the Prevention and Treatment of Multiple Sclerosis:

4.2.1.Bee venom:

The honey bee venom contains a wide variety of heavy and light chain peptides. It also contains phospholipase A2, apamin, melittin, and adolpin, among other proteins. It has anti-inflammatory effects.

[41]According to a recent study, the structure of separated myelin is adversely affected when exposed to the venom enzyme phospholipase A2, which is present in bee venom and other venoms.[42] In two clinical trials, the effects of bee venom on MS patients were investigated. The results showed that bee venom did not improve the quality of life, fatigue, or impairment of MS patients.

4.2.2.Lipoic acid:

A natural antioxidant called lipoic acid is present in many foods. The main sources of lipoic acid include yeast extract, spinach, broccoli, liver, kidney, and hearts. Studies have shown that lipoic acid is useful in treating diabetes, neurodegeneration, and the harm caused by ischemia-reperfusion.[43]

This drug has been put to the test on MS patients in a few clinical investigations. A decrease in pro-inflammatory cytokines was observed in MS patients who took 1200 mg of lipoic acid daily, according to additional study. The effectiveness of lipoic acid in treating MS patients is presently the subject of numerous clinical investigations. To learn more about how lipoic acid impacts MS patients, however, more study with bigger sample sizes is required.

4.2.3.Sesame oil:

Asian countries have long viewed sesame seed as a staple food with nutritional value. Sesame oil has a potent anti-inflammatory mediator and lipid peroxidation inhibitor.

We came across two articles from the same research team that demonstrated how administering EAE sesame oil to mice orally[44] and intravenously decreased behavioral deficits and improved immune system function. The advantages of sesame oil have been studied in several clinical trials for diseases including hypertension, allergy, and inflammation, but no research has been done on MS patients to far.

4.2.4.Erhuangfang :

Erhuangfang administration reduced behavioral impairments, inflammatory response, and demyelination in the CNS of mice with EAE. The Beijing Food and Drug Administration subsequently authorized it as a hospital preparation. (No. 10003). Erhuangfang dramatically decreased relapse rate and stopped MS development, according to a 2-year prospective. The researchers once more recommended this medicine as a successful treatment for MS relapses.[45]

4.2.5. *Tripterygium wilfordii hook f*:

Herbal medicine uses *T. wilfordii Hook F.* Rheumatoid arthritis has been treated with it in conventional Chinese medicine. Triptolide, 5-hydroxytriptolide, and tripchlorolide are the three main substances with immunosuppressive and anti-inflammatory effects that have been identified from this plant.

According to Fu et al., triptolide analog 5-hydroxytriptolide (1 mg/kg/day) prevented EAE. Additionally, it reduced the growth and activation of T cells[46]. In line with this, triptolide oral dosing (100 mg/kg) resulted in both preventative and therapeutic benefits in mice with EAE. Tripchlorolide (40 g/kg) also had comparable results.

4.2.6 Hesperidin :

It is a natural flavonoid that is abundant in citrus species such as lemon and orange. Various biological properties have been reported for hesperidin including anticancer, antiviral, and antiinflammatory activities.[47]

The therapeutic effects of hesperidin in diseases other than MS have been evaluated extensively in clinical studies. However, there is no clinical trial on patients with MS.

4.3.Discussion:

The drugs that are currently on the market cannot completely reverse the persistent myelin damage caused by MS. Natural products have shown exceptional therapeutic benefits on MS in terms of anti-inflammation, immunological management, nervous system protection, nervous system mending, and BBB protection. Currently, various Natural products have previously been used in clinical studies for the treatment of autoimmune diseases, including sinomenine for the treatment of rheumatoid arthritis. Herbal drugs may be helpful in treating MS and its symptoms by reducing adverse effects.

Other symptoms including fatigue, depression, pain, and cognitive issues can be treated naturally without having any negative side effects.

The results of the most recent study show that natural products are very efficient and have tremendous promise for treating MS. Furthermore, it is crucially necessary to understand the many processes by which natural compounds cure MS. Currently, it is clear from the references that the general processes of natural products include anti-inflammatory, immunological modulation, neuroprotection, nervous system repair, and BBB protection. Some natural compounds have the ability to control both inflammation and the immune system. Some even do neuroprotection and nervous system repair at the same time, in addition to having various roles. The primary action of anti-inflammatory drugs is to lower the concentration of inflammatory factors. Anti-inflammatory action is crucial for treating MS because it protects the CNS from ongoing damage. Natural substances can prevent inflammatory cells from invading the CNS and reduce microglia activation, preventing the CNS from suffering long-term harm.

Natural products have a remarkable ability to regulate the immune system both in vivo and in vitro. NPs have sufficient benefits despite the complicated immune response in MS. This

positive outcome, nevertheless, cannot exclusively be attributed to immunoregulatory factors. The EAE model exhibits BBB disruption along with a loss of tight junction proteins .

Natural remedies can provide protection when the nervous system is harmed.

The need for novel drugs to treat MS is essential given that the treatments for the disease that are now available do not directly stimulate repair[48].NPs can also encourage the development of neural stem cells .

In conclusion, NPs have a multi-pathway, multi-target, and synergistic impact of several mechanisms to work together to perform a therapeutic role in MS therapy.



Chapter-5

5. Conclusion:

The medications now available on the market cannot fully treat Multiple sclerosis since it results in permanent myelin damage. While natural products have demonstrated a superb ability to treat Multiple sclerosis in terms of anti-inflammation, immunological control, nervous system protection, nervous system mending, and BBB protection. Some natural products are currently being utilized in clinical trials to treat autoimmune illnesses. We believe that the use of natural products has the potential to significantly advance Multiple sclerosis therapy in the future, and that additional research into the potential therapeutic impact of natural products on Multiple sclerosis is very beneficial.



Chapter-6

6.Reference:

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