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Current trends in Natural Management of Multiple Sclerosis

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ABSTRACT

The disease that affects the myelin sheaths that surround nerve cells within spinal cord and brain is multiple sclerosis (MS). The only disease-modifying treatment for primary-progressive MS that has received FDA approval is ocrelizumab (Ocrevus) (DMT). This treatment slightly reduces the likelihood of progression compared to no treatment. Significant health hazards are associated with several of the disease-modifying treatments used to treat MS. Many MS patients employ a variety of complementary or alternative therapies, or perhaps both, to assist manage their symptoms. Although there are few studies to support its utility in controlling MS symptoms, physical and mental health can be enhanced through a variety of practises, some of which are: working out, meditating, doing yoga, getting a massage, eating right, trying acupuncture, and learning to relax. Physical therapy can be used to treat MS and alleviate symptoms such as leg weakness and gait issues. Numerous herbs aid in the treatment of MS which reduces its side effects and symptoms. Multiple studies firmly demonstrate that the anti-inflammatory and anti-oxidant components in medicinal plants naturally have a therapeutic significance for multiple sclerosis. Goal of this paper is to highlight the favourable features of various treatments in managing or treating the symptoms of MS.

INTRODUCTION

Multiple sclerosis (MS) can cause dysfunction in the spinal cord and brain (central nervous system). Encephalomyelitis (MS), another name for the disease, spreads. Here the protective sheath shielding the nerve fibers (called myelin) is attacked by the immune system, as a result the brain's ability to send and receive signals are disrupted. Nerve degeneration or permanent impairment may develop as a result of this condition [1]. The inability of the damaged nervous system to relay messages results in a wide range of physical, psychological, and occasionally psychiatric symptoms [2,3]. The effects of multiple sclerosis are unpredictable and can range from mild impairment to the complete loss of a patient's capability to walk, try writing, or communicate.

There is no single pathognomonic marker for MS, which is a very heterogeneous disease with clinical patterns unique to each patient. Although there isn't any proof of a specific agent, infection has long been considered a potential MS trigger. Recently, the idea of pro-inflammatory gut microbial environment as a trigger of autoimmunity must have emerged, with possible implications of dysbiosis being established in MS based on pre-clinical research in its purported animal studies, experimental autoimmune encephalomyelitis (EAE).

There are several courses of Multiple sclerosis that are described below:

Remitting-relapsing MS, secondary progression MS, primary progression MS and progressive-relapsing MS [4]

AETIOLOGY

Numerous hypotheses are being considered by researchers as to why the immune system targets the myelin sheath in the brain which included:

Combating an infectious agent (like a virus) that contains components which resemble brain tissue (called molecular mimicry)

Eliminating unhealthy brain cells via destroying them

Mistaking foreign cells for regular brain cells

The BBB is another feature that keeps the immune system out of spinal cord and the brain. The immune mechanism has access to brain if this barrier is breached. When this occurs, the immune system could mistakenly see brain tissues like myelin as "foreign."

According to research [5], MS may be driven on by genetic predispositions mixed with environmental variables.

Genetic predisposition:

Although susceptibility to MS may be inherited, MS itself is not hereditary. According to studies, some people with MS have one or more MS-positive family members or relatives.

According to recent studies, MS vulnerability may result from a combination of dozens of genes and possibly hundreds of mutations in the genetic code (known as gene variants). These genes have been discovered to some extent, and the majority of them are linked to immune system operations. Numerous genes that have been discovered with the patients having various autoimmune disorders that includes rheumatoid arthritis, type 1 diabetes, or lupus share similarities with many of the known genes. [6].

MS is thought to involve many genes. In case a parent or a sibling has MS, the chances of developing the condition is marginally increased.The lifetime chance of developing MS is thought to be roughly 3% if one of your parents or siblings develops [7]. The likelihood that somebody will acquire MS ranges from 0.1 to 0.3 percent on average.

MS victims also have family members who have the disease. To demonstrate this, 2014 cohort research [8] tracked 150 MS people to discover if their relatives also acquired the disease. Over a 35-year period, the researchers discovered that 49 out of the 150 people (32.7%) reported having at least one cousin with MS. There were 86 relatives in total who were affected.

Environmental factors:

According to several studies, persons who spend more time in the sun and have relatively greater vitamin D levels are less likely to get MS, have a milder course of the disease, and experience fewer relapses. Vitamin D is produced by human skin in bright sunshine. According to research, vitamin D may assist in immune system regulation in ways that lower the risk of MS or general autoimmune disease. Persons from equatorial locations, where there is a lot of intense sunlight, are typically considerably less likely to develop MS than people from temperate countries, like the United States and Canada.

Smokers are more likely to get MS and to experience a more severe course of the disease, according to studies. Indeed, compared to non-smokers, smokers frequently experience higher brain lesions and shrinkage. The causes of this are not yet apparent. [6]

Environmental factors are things that come into contact with in the environment. MS threat has been connected to a number of environmental factors. A few of these are:

> Low levels of vitamin D or sun exposure

> Air toxicity

> Ccontact with organic solvents

On a review [9] of these parameters identified low vitamin D or little sun exposure as moderate environmental risk factors for MS. It was thought that there was a lesser correlation between organic solvents and air pollution.

PATHOPHYSIOLOGY

AUTOIMMUNITY

MS a cell-mediated auto - immune disease affecting CD4+ & CD8+ cells hence attacking central nervous system (CNS) myelin antigens. It's possible that autoantibodies aid or boost the body's natural defences. Normal people have auto-reactive T cells that are directed towards myelin components; these cells do not cause disease but do have benefits for the brain.

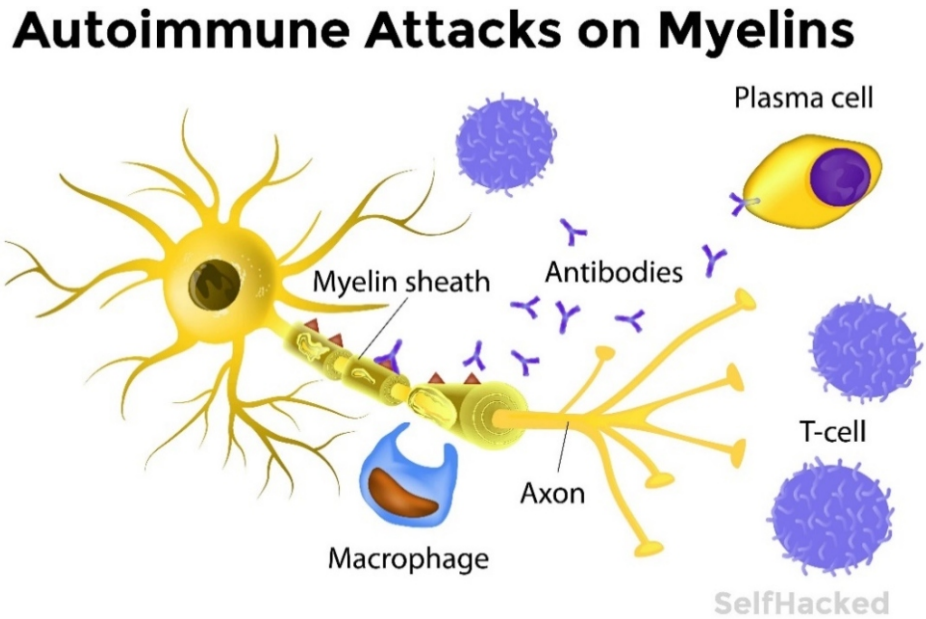

Fig. 1 : Source: https://medium.com/@mstreatment/multiple-sclerosis-risk-factors-dafc58824961.

Myelin-autoreactive T cells, specifically Th17, Th1 & CD8 cells are the true culprits in development of the disease. The MS pathogenesis are influenced by B & T cell interactions between peripheral and CNS. As a corollary, there are three key locations where pathogenic B and T cells converge to influence MS disease progression [10,11,12]. How Epstein-Barr virus (EBV) can affect MS development is the subject of numerous ideas [13]. Since MS patients have impaired B-cell tolerance, EBV-infected B cells are able to evade suppression by T regulatory (Treg) cells and CD8+ in secondary lymphoid organs [14,15,16]. Disease - causing memory B cells are developed when activated B cells gain entry to germinal centres (GCs) as well as engage with follicular T helper cells [17]. As result of the action of IFN-γ, IL-21& B cells undergo a differentiation into T-bet-expressing memory cells, which in turn activate Th effector cells like Th17 [18,19]. One of the primary pathogenic Th effector cell types responsible for the emergence of numerous autoimmune disorders has been identified as Th17 cells [20]. These subsets are more likely to invade MS patients' central nervous systems (CNS) because they express different chemokine receptors (CXCR3, CCR6), adhesion molecules (VLA-4), and pro-inflammatory cytokines [21, 22].GM-CSF-, IFN-γproducing T &memory B cells of T-bet+ are likely to interact within follicle-like structures within the CNS, leading to clonal proliferation inflammation and demyelination [23]. Memory B cells of T-bet+ continue to differentiate inplasma blasts or plasma cells, which release large quantities of potentially devastating antibodies (oligoclonal bands) that provoke intense reactions in the brains of people with MS [24, 25, 26]. Hence, it appears that lesion initiation and development in MS condition are influenced by dysregulation of multiple cell types of the adaptive immune system.

REACTIVE OXYGEN SPECIES (ROS): Functional impairments might result from increased ROS production that contributes to axonal/neuronal damage, demyelination, release of pro-inflammatory cytokines, BBB integrity modification and interactions with proteins, lipids and nucleic acids [27-32]. Although oxidative stress can cause inflammation and vice versa, in MS patients, oxidative stress comes first [33]. However, the generation of ROS might be viewed as an initiating stage of MS pathophysiology.

INFECTIVE PATHOGENS: Pathogenic T-cells that are reactive to myelin are strongly induced by infectious pathogens. Possible causes include: cross-reactivity with CNS myelin antigens; activation of existing developed autoreactive immune repertoire; or self-limited brain infection that releases myelin antigens. The CNS may become ill and demyelinate as a result of a chronic viral infection. Subacute sclerosing pancephalitis (SSPE) is an inflammation of the gray and white matter caused by a sustained progressive infection of the CNS with the pathogenic virus. In the CNS of patients with SSPE, the virus has been found in immunological, glial, and neuronal cells [34].

MICROBIOME: It has demonstrated by numerous research [35] that MS patients have intestinal dysbiosis. Some MS patients experience increased bodily inflammation due to certain gut flora. Changing the gut microbiome has been shown to ameliorate some MS-like symptoms in experiments on animals [36]. Dysbiosis is the term for when any of the colonies in your gut microbiome are out of equilibrium. Different digestive symptoms might be brought on by dysbiosis. It contributes to the emergence of numerous auto immune [37] illnesses. Strong protective walls prevent bacteria from seeping [38] from the gut into the bloodstream and the rest of the body. Dysbiosis of the gut creates openings in this wall that allow the microbiome to leak, which in turn induces inflammation and is connected to autoimmune disorders, like MS [39].

MANAGEMENT OF MULTIPLE SCLEROSIS:

ROLE OF HERBAL THERAPY:

Despite the fact that there is no medication or dietary supplement that may completely cure MS, several treatments can help patients control or decrease the disease's progression. Other treatments have the ability to drastically lessen symptoms or lengthen remission times. When Western medicine fails to relieve their problems, many people resort to alternative therapies. Others opt to try learning about the possibilities of complementary therapies.

Herbs:

Turmeric: The tropical plant Curcuma longa L. is native to the warm climates of Southern and Southeastern Asia. The Zingiberaceae family, of which ginger is a part, also includes C. longa. A number of studies have looked into curcumin's anti-inflammatory properties that were found primarily mediated by two mechanisms: (1) blocking the pro-inflammatory cytokines production (2) blocking Th-17 difference and associated pathways [40, 41]. Studies on animal models have shown that curcumin is effective in reducing MS symptoms by, among other mechanisms, preventing the spread of invading inflammatory cells in CNS[42], modifying the inflammatory process by decreasing the pro-inflammatory & inflammatory cytokines expression, lessening the MS symptoms by blocking the IL-12 signalling pathway in T-cells & treating the EAE model of MS using polymerized form of nanocurcumin, that demonstrated antioxidative and anti-inflammatory activity with increased remyelination and decreased EAE score [43, 44].

Saffron: Crocus sativus (L.) belonging to Iridaceae family, saffron is produced by a flowering plant. Saffron has been known for its ability to treat a number of medical conditions, especially those affecting the digestive system [45]. Crocin reduces neurological damage in experimental autoimmune encephalomyelitis (EAE) by decreasing syncytin-1, oligodendrocyte cytotoxicity and NO-induced astrocyte via its anti-inflammatory effect [46,47]. Increased expression of Syncytin-1 was observed in microglia, astrocytes and glial cells in multiple sclerosis lesions [48].

St. John's Wort: Also known *Hypericum perforatum* L., a flowering plant of Hypericaceae family. Although *H. perforatum* is native to Asia &Europe, it is now found worldwide [49]. Due to its wide spectrum of therapeutic benefits for conditions like depression, anxiety and menstrual disorders, *H. perforatum* has been a well-known herb since antiquity [50]. Currently, *H. perforatum* is utilised to treat malignancies [51], neurological diseases [52] & disorders associated to inflammation [53].

Ginger: *Zingiber officinale* Roscoe (Zingiberaceae), a fragrant plant, native to India. *Z. officinale* is also widely cultivated in Latin America, tropical Africa, and Asia [54]. Recent research has shown that ginger has anti-cancer [55], antioxidant [56] & anti-inflammatory[57] properties. By preventing NF-jB activation, 10-gingerols reduced the generation of proinflammatory cytokines and LPS-induced NO [58]. Ginger is consumed by MS patients because of its two active components proved for its anti-inflammatory properties.

Cranberry: *Vaccinium macrocarpon* (Large Cranberry), native of North American species(family - Ericaceae). The fruit of the *V. macrocarpon* is used to make cranberry juice [59]. A few clinical investigations [60] have looked at the prevention of UTIs in MS patients by cranberries.

Ginseng: *Panax ginseng*(Asian ginseng) is a traditional plant medicine of Asia (family -Araliaceae)[61]. It is also among the most effective medicinal herbs for treating a variety of neuroinflammatory disorders that includes Alzheimer's disease, Huntington's disease, Parkinson's disease and MS[62]. Ginseng decreased severity of EAE by: inhibiting T cell proliferation, inhibiting inflammatory cytokines (FN-, IL-1, and IL-17) production and depleting CD25+ cells [63]. As a result, it was concluded that ginseng was effective in treating MS-related fatigue and improving the life quality in such patients.

Valerian: *Valeriana officinalis* L. (family- Caprifoliaceae) native to parts of Asia, Europe and North America [64]. The primary factor causing fatigue in MS patients is sleep disruption [65]. Valerenic acid, a key component of *V. officinalis* root extract, has been shown in clinical studies to be useful in treating sleeping disorders from mild to moderate [66]. Valerenic acid has a special affinity for the $GABA_A$ receptor, similar to benzodiazepines, which are GABA analogues.

Agrimony: Belonging to Rosaceae family is native of Europe and North Africa is common agrimony, often known as church steeples (*Agrimonia eupatoria*) [67]. Although various agrimony species are said to have diverse medicinal characteristics, new study has found that some of them also have antiviral [68], antioxidative, anti-inflammatory, and metabolism-boosting [69] capabilities.

Echinacea: *Echinacea purpurea* commonly called as coneflowers (Asteraceae) is native of Easter and central northern America [70]. The plant was historically been used to treat upper RTI, including colds. Other qualities of the plant extract, such as its ability to reduce inflammation and promote the growth of new tissue [71], show great potential for improving the life quality of MS patients.

Dandelion: *Taraxacum officinale* (Asteraceae) native of Eurasia and North America also available worldwide which is being used in Korean herbal system of medicine. Roots & leaves of the plant are claimed to have therapeutic benefits. Dandelion has shown in studies to have antioxidant and anti-inflammatory effects that are beneficial to MS patients [72]. Additionally, it has the ability to lessen fatigue, the key symptom of MS [73].

Bilberry: *Vaccinium myrtillus*(huckleberry) native to Europe, is a relative of blueberry and its fruit or leaves are used [74]. Decrease in several immunoregulatory and NFκB-regulated proinflammatory chemokines was observed in healthy subjects who took Medox (commercial product of Bilberry) for 3 weeks[75]. Myrtocyan® (commercial bilberry extract-200 mg/kg) has been shown to improve vision, short-term memory& control of sensory input in rats, and it also increases triiodothyronine transport to various brain regions. [76,77].

Milk Thistle: *Silybum marianum* (Family- Asteraceae) native of Mediterranean region of Europe, including Greece, Afganistan and Iran [79]. Milk thistle may modulate the immune system [80] in MS and help MS medications work better, but more research required to carried out before the herb is officially recommended for MS treatment.

Herbal extracts:

Melilotus officinalis is commonly known as sweet clover (family - Fabaceae) native of Eurasia and later established in North America, Africa and Australia [81]. In an investigation using EAE model of the disease, *Melilotus officinalis* herbal extract's therapeutic potential for treating multiple sclerosis was principally examined. Administration of *Melilotus officinalis* as a preventative measure lessens the disease's clinical symptoms. Gene expression of proinflammatory cytokines, including those of IFNγ, TNFα &IL-6, were markedly reduced. The results revealed that the medicinal efficacy of this herbal extract in the treatment of MS [82].

Thymus vulgaris which is commonly known as Thyme (family - Lamiaceae) is native of southern Europe from the Western Mediterranean to Southern Italy. In cohort study, its modulatory effects were examined in relation to the histopathological scores, clinical symptoms and production of several proinflammator and anti-inflammatory cytokines in EAE model, that includes IL-4,TGFα and IL-10. The work demonstrated that thyme extract immunomodulatory effects in the EAE model can be considered in future studies for treatment of MS [83].

Glycyrrhizae Radix- Roots of Glycyrrhiza glabra commonly called Licorice (family -Fabaceae) distributed in Asia, Australia, Europe. A study examined the immunomodulatory effects of ethanolic extract on autoimmune reactions using mouse microglia BV2 cell line, primary mouse splenocytes (SPLC) and an EAE mouse model. The initial research on the immunomodulatory effects of the extract on antigen-specific SPLC responses in EAE helped to find therapeutic options by focusing on IFN-γ related autoimmune reactions for MS therapy [84].

Achillea millefolium is commonly known as Yarrow (Asteraceae) native of Europe, Northern Hemisphere in Asia and North America [85]. Less brain inflammation. In EAE-induced mice, aqueous *A.millefolium* extract reduced demyelinating lesions, inflammatory responses & disease severity. EAE-induced mice had higher TGF- levels [86].

Herbal Compounds:

Resveratrol (IUPAC - 3,5,4′-trihydroxy-trans-stilbene): Plants produce resveratol in response to damage or pathogens like bacteria and fungi; it is stilbenoid, a phenol, and phytoalexin. Resveratrol can be found in foods like grape skins, raspberries, mulberries, blueberries, and peanuts [87]. Resveratrol is a polyphenol that shown the remyelination-related protein Olig1 had its expression boosted. This study has the potential to be the first to demonstrate the pro-remyelinating effect of resveratrol, suggesting its potential use in MS treatment.[88].

Scutellarin is a flavone (IUPAC - 4′,5,6-Trihydroxyflavon-7-yl -D-glucopyranosiduronic acid), a phenolic chemical molecule from *Scutellaria barbata* and *S. lateriflora*. Scutellarin protects estrogen-damaged nerve cells [89]. Cohort research [90] on scutellarin showed it protects neurons from injury and promotes neurogenesis, suggesting it could cure neurodegenerative illnesses. As neural stem cells can become oligodendrocytes produced by myelin, the compound could be used for MS treatment.

Hyperforin (IUPAC - 1R,5S,6R,7S) -4-Hydroxy-6-methyl-1,3,7-tris (3-methylbut-2-en-1-yl) -6-(4-methylpent-3-en-1-yl) -

5-(2-methylpropanoyl) bicyclo [3.3.1] non-3-ene-2,9-dion), generated by *Hypericum perforatum* (St John's wort). It may have antidepressant effects due to hyperforin [91]. A study used [92] hyperforinloaded gold nanoparticle to treat EAE model. Hyperforin & Hyp-GNP found to reduce EAE clinical severity and spinal cord inflammation. It's more effective at treating EAE than free hyperforin.

Astragaloside IV is a natural saponin and active principle (IUPAC - 3-O-beta-D-xylopyranosyl-6-O-beta-D-glucopyranosyl- cycloastragenol).*Radix astragali* commonly called milkvetch (dried root of *Astragalus membranaceus*). It is a famous for numerous disorders intraditional Chinese Qi-tonifying herbs[93]. Giving a dose of 20mg/kg per day, the compound decreased the severity of EAE in mice. ASI can be used for clinical therapy and or prevention of MS [94].

Guggulsterone is a phytosteroid [IUPAC- (8R,9S,10R, 13S,14S)-17-Ethylidene-10,13-dimethyl-1,2,6,7,8,9,11, 12,14,15-decahydrocyclopenta [a] phenanthrene-3,16-dione] discovered in the guggul plant resin, *Commiphora mukul*. E- and Z-guggulsterone are stereoisomers of guggulsterone[95]. Chronic treatment of GST for about 28 days improves behavioural impairments (motor coordination, spatial cognition memory and grip) which is associated with reduced STAT-3 levels. Raising myelin basic protein levels and PPAR-γ in rat brain supports both signalling pathways. Long-term GST therapy restores Bcl-2 and gross morphological changes. GST may be a contender for treating MS-related motor neuron dysfunctions. [96]

Acetyl-11-keto-β-boswellic acid (AKBA) from *Boswellia serrata*, chemically is an active pentacyclictriterpenoid that possess anti-inflammatory & antioxidant properties [97]. In animal model of MS, researchers looked at the levels of Nrf2/HO-1 in the brain to determine whether or not AKBA had any preventative effects on behaviour patterns, molecular, neurochemical, gross histopathological changes. Accordingly, AKBA increases Nrf2 & HO-1 expression in rat brain. It helped restore neurochemical levels, which in turn halted the worsening of MS. [98].

Role of Natural Anti-Oxidants:

The antioxidant response elements (ARE) & transcription factor nuclear factor-E2-related factor (Nrf2) in the genes encoding antioxidant enzymes regulate the majority expression of antioxidant enzymes, and oxidative stress induces these expression patterns. Increased expression of Nrf2/ARE-regulated antioxidants in MS patients' brain tissue is indicative of the presence of oxidative stress in these lesions. Hence, antioxidant therapy might be a desirable MS treatment. It would be intriguing to use activators of the Nrf2/ARE pathway to induce endogenous enzymatic antioxidants in order to achieve sufficient antioxidant levels to obstruct the pathogenic processes driving the development of MS lesions.

Omega 3 fatty acid:

Multiple sclerosis patients were found to have lower levels of polyunsaturated fatty acid (PUFA), antioxidants & impaired cellular antioxidant defence mechanisms. Omega-3 fatty acids come from marine and plant sources and have a long chain length and a polyunsaturated fat composition. After 6 months of supplementation with long chain omega-3 PUFAs (6 g/day; 86% EPA + DHA), the secretion of pro-inflammatory cytokines, IL-1b, TNF-α, IL-2, and IFN-γ by stimulated peripheral blood mononuclear cells was lower in MS patients than in healthy controls [99].

Vitamins:

Studies showed that antioxidant vitamins (retinol, β-carotene, α-tocopherol and ascorbic acid) are depleted in MS patients' sera during an attack. This depletion may very well related to increased oxidative burden as shown from lipid peroxidation products.[100]. One of the most important antioxidants "chainbreakers" is alpha-tocopherol (vitamin E). Vitamin E has indirect anti-inflammatory properties in addition to direct neuroprotective antioxidant actions. Vitamin E blocks the effects of LPS-induced p38 MAPK and NfκB signalling, which are required for microglial activation [101]. Retinoids, which are chemicals made from vitamin A, cause the immune system to switch from Th1-type responses, which include the release of interferon gamma, to Th2-type cell-mediated responses. These characteristics offer a rationale for clinical trial of interferon beta-1b and RA retinoids combined therapy in MS patients [102,103].

The sun-derived hormones (1,25- dihydroxyvitamin D3 and vitamin D3) could lower the risk of autoimmune-mediated neurodegenerative and chronic CNS inflammatory illness.[104]

Flavonoids:

Many foods, including fruits and veggies, grains, teas and wines, contain flavonoids, chemicals with anti-inflammatory and antioxidant effects [105]. In human and animal studies of demyelinating disease, supplementation with flavonoids, especially the green tea tannin such as epigallocatechin gallate (EGCG), has been associated with significant improvements in illness outcomes like cognitive functioning and anxiety, which are thought to be overwhelmingly driven by antioxidant activity. [106, 107] Clinical trials have examined the effect of cocoa, with its high natural flavonoid content, on multiple sclerosis symptoms. Intake of flavonoid-rich cocoa was found to alleviate day-long fatigue in these studies [108, 109].

Role of Probiotics:

Probiotics are constituted of important microbial species that can regulate the immune reactions of the host organism in a healthy way by creating bacteriocins, which function as antimicrobial agents[110]. The two main phyla of a healthy gut microbiota are Bacteroidetes and Firmicutes. In MS, the gut microbiome changed. In MS patients, probiotics can naturally trigger the anti-inflammatory peripheral immune response. Probiotics can modify the gut microbiome, which is helpful for treating MS. [111]

Probiotics on MS inflammation: Probiotics [Lactobacillus (4 strains), Bifidobacterium (3 strains), and Streptococcus (1 strain)] were given to RRMS patients in a study [112]. In addition to discovering changes in the composition and function of gut bacteria, the researchers discovered a link between probiotic use and a decline in the number of monocytes, an immune system cell in MS patients. Specifically, these monocytes had a higher & lower expression of anti-inflammatory genes &pro-inflammatory genes respectively. In light of this, scientists hypothesised that probiotic administration could change the gut microbiome and, as a result, soothe the immune system, possibly even preventing its attack on MS patients' nerve systems.

Probiotics on MS disability: Expanded Disability Status Scale (EDSS) scores and Beck Depression Inventory (BDI) scores were used in a double-blind study [113] to assess how

probiotic supplementation affected both depression and disability. It was discovered that the probiotic participants had improvement in EDSS and depression scores in comparison with those of placebo group. Probiotics were said to benefit both the physical and emotional health of someone with MS, including their ability to walk.

CONCLUSION

Since there is no known cause or treatment for multiple sclerosis (MS), medicines should ideally focus on both treating symptoms and slowing the disease's progression. Traditional treatments have only attempted to prolong the disease's remission phase by calming the hyperactive immune response that characterises the relapse stage. Now, until ten years ago, there were no effective choices for slowing the progression of the disease; however, more recent research has clarified the role of interferons and other immunosuppressant medications. Interferons appear to do this rather successfully to start with, functioning to lower the inflammatory response and prevent additional neuronal damage. Drug therapy seeks to counteract the harmful effects of the overactive immune response experienced in MS. Unfortunately, because to their adverse effects and cost, it is important to consider the role of complementary therapies in MS treatment. The potential for treating neurodegenerative diseases like Parkinson's and MS has been expanded thanks to medicinal plants. According to a review of the literature, herbal remedies may help cure MS and its associated symptoms by promoting remyelination, lowering demyelination, and reducing CNS inflammation. Therapeutic benefits in MS disease are primarily attributable to medicinal plants' anti-inflammatory and anti-oxidant properties, which serve to mitigate the condition's clinical manifestations and associated neuropathological alterations. Reviewing the information presented above, one might reach this verdict. Most of the time, the anti-inflammatory effects of medicinal plants are accomplished by blocking the entry of inflammatory cells into the brain, which in turn reduces the production of pro-inflammatory and inflammatory cytokines. More study is needed to determine the precise mechanisms through which medicinal herbs exhibit their neuroprotective and anti-inflammatory effects. Since most MS herbal therapy research has been performed on experimental animals, clinical trials of these studies would require to be approved before these herbs could be recommended to MS patients. Other positive effects of medicinal plants on MS patients include drowsiness, better sleep, antidepressant effects, relief from muscle stiffness, and a decrease in bladder disruption. These effects are in addition to their neuroprotective effects. The immune system and gut flora are linked, thus probiotic supplements can be recommended for MS patients.

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