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Momordica dioica: Phytochemistry, Traditional Uses and It's Neuroprotective Activity

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ABSTRACT

***Momordica dioica* Roxb. ex Willd. (being spiny gourd or teasel gourd) is a climber plant of Cucurbitaceae family, which is extensively found in tropical and subtropical parts of Asia. Historically, it has been used in different native healing of health conditions like diabetes, inflammation, liver disorder, gastrointestinal conditions and reproductive problems. The paper is going to examine the chemical composition of phytochemicals, ethnomedicinal significance and neuroprotective potential of *M. dioica* against the background of modern pharmacological literature. Phytochemical studies indicate that a wide variety of bioactive chemicals are contained in M. dioica, with traces of flavonoids (quercetin, kaempferol), phenolic acids (gallic acid, ferulic acid), triterpenoids (ursolic acid, oleanolic acid), saponins, alkaloids, glycosides, and essential micronutrients. These compounds add to the broad pharmacological actions of the plant that include antioxidant, anti-inflammatory, antidiabetic, antil-micros and hepatoprotecs. Especially notable among them is the neuroprotective effect of *M. dioica*, ascribable to its actions on reducing the impacts of oxidative stress, inhibiting neuroinflammation, regulating cholinergic transmission, and enhancing neuronal survival. Based on preclinical studies, M. dioica may alleviate neuronal injury, improve memory task-performance, and prevent neurodegeneration by a variety of molecular pathways. These results are consistent with old knowledge, but there is only a clinical confirmation of these, which is only limited, and such information requires additional research that needs to be conducted on bioassay-guided isolation, pharmacokinetics, and human tests. Finally, *Momordica dioica* is an encouraging medicinal herb that possesses multi-targeted pharmacological effects and has a beneficial impact as a future therapeutic agent in neurodegenerative processes. Concluding this review, in the modality of incorporating both traditional use and modern scientific validation of plant-based therapeutics to build an environment of safe, effective, and cost-effective drug development to the field of neuropharmacology and the entire science of biomedicine deserves consideration.**

Keywords- *Momordica dioica*, Phytochemistry, Neuroprotective activity, Ethnomedicinal uses, Antioxidant properties, Traditional medicine.

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I. INTRODUCTION

Medicinal plants have been a challenging topic of ongoing and extensive research since they are considered as therapeutic agents in pharmaceutical sciences and ethnomedicine. Intended among them is *Momordica dioica* Roxb. ex Willd, which features significantly in the family of Cucurbitaceae because of its complex pharmacological properties and long alleviation within customary medicine. Known by various names such as spiny gourd, teasel gourd or the dioecious climbing herb, *M. dioica* is a perennial, dioecious climbing weed whose chief tendencies are located in India, Nepal, Bangladesh as well as parts of Southeast Asia. Throughout centuries, the plant has been closely intertwined into the cultural and pharmacological heritage of many natural healing systems like Ayurveda, Siddha and folk medicine. As the interest in the production of plant-derived pharmaceuticals keeps growing, *M. dioica* has become an object of particular research with its high variety of phytochemicals and bioactive potential, particularly in the case of neurological conditions [1].

Neurodegenerative disorders including Alzheimer diseases (AD), Parkinson diseases (PD), and other diseases of the central nervous system (CNS) still exert an immense health burden in the world. Such diseases are also typified by a gradual degradation of the neuronal structure and functionality eventually following to cognitive and functional impairment. Although innovations in the neurobiology and development of therapeutic drugs, existing pharmacotherapies of such disorders mostly relieve the symptoms and are accompanied by side effects, poor efficiency and have high rates of relapse. Therefore, there is an urgent imperative to find and conceptualize other methods of therapy that are less harmful as far as side effects are concerned and with more efficacy. The importance of the natural products, especially those of the medicinal plants that have high antioxidant, anti-inflammatory, and neuroprotective effects as potential neurotherapeutic agents has received wide recognition within the last few years [2].

The conventional application of *M. dioica* has historically been numerous medical uses regarding disease control like diabetes, inflammation, bowel complaints, infection and reproduction matters. This claims by ethnobotany have been reinforced by little but accumulating preclinical and experimental evidence about the antioxidant, anti-inflammatory, hepatoprotective, and antimicrobial activities of the plant. In further recent past, the neuro protective efficacy of M. dioica has created a flurry of interest due to identification of the possible phytoconstituents like flavonoids, triterpenoid, saponins, alkaloids, and phenolic compounds. These bioactives show profound potential as to their impact on the health of neurons, in part by ameliorating oxidation stress, preventing neuroinflammation, and regulating neurotransmitters, giving them a multi-faceted potential to counter the neurodegeneration process [3].

The neuroprotective value of *M. dioica* can be especially important considering the multifactorial character of the pathologies of the neurodegenerative diseases. Deposition of reactive oxygen species (ROS) toxicity and neuronal oxidative damage along with mitochondrial dysfunction, release of pro-inflammatory cytokines and excitotoxicity are the main molecular mechanisms involved in neuronal death and CNS dysfunction [4]. Research has proved that the phytochemicals contained in *M. dioica* can have free radicals, stimulate endogenous antioxidant enzymes, inhibit expression of certain inflammatory markers, like TNF and IL-6 and prevent damage to neuronal homeostasis in many instances. This has projected *M. dioica* as having a prospect of having neuroprotective formulations and phytopharmaceuticals development against the prevention and management of neurodegenerative diseases.

Pharmacognostically all the parts of the plant i.e. the roots, leaves, fruits and seeds have some medicinal value but mostly used medicinally are the fruit. Phytoconstituents separated on various portions of the plant have been identified with the sophisticated methods of analysis including high-performance liquid chromatography (HPLC), gas chromatography-mass spectrometry (GC-MS), nuclear magnetic resonance (NMR) spectroscopy and liquid chromatography-tandem mass spectrometry (LC-MS/MS). These researches have clarified how different secondary metabolites with substantial pharmacological importance exist. There is also solid documentation of the neuroprotective and cognitive-enhancing capabilities of flavonoids like quercetin and kaempferol, and triterpenoids as well as saponins have displayed potential to influence synaptic plasticity and minimize neuronal swelling [5].

In addition, the anti-inflammatory effect of the *M. dioica* would also play an important role in the face of neurodegeneration, which is evident in the fact that chronic inflammation intensifies the destruction of neurons and promotes the rapid progression of the disease. Inhibition of inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) by the bioactives of *M. dioica*, supports its therapeutic applications in neuroinflammatory disorders. Adding such effects to the antioxidant and mitochondrial protective effects leads to a cerebral protective mechanism which goes much beyond what is known so far and which is worth exploring in future scientific research [6].

Besides experimental research, traditional use and ethnomedical insight give relevant basis of the pharmacological prospective of *M. dioica*. The plant is used as medicine and food in the rural and tribal communities around India and other surrounding nations. All the fruits are used in regular diets in the monsoons as it is said to boost immunity and maintain the stomach health. The root or the leaf extracts are used to make herbal preparations which are used to treat fevers, respiratory disorders and female reproductive health problems [7].

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The therapeutic possibilities of *M. dioica* can be seen to gain more and more acceptance, but some obstacles still exist on the way to transferring the traditional application and its experimental results into the clinically proved interventions. Among the major limitation is the fact that there are no exhaustive studies concerning its safety, efficacy, pharmacokinetics and standardization of doses in humans. Also, geographical, seasonal, and environmental influences on the variability of phytochemical content are a problem to the effectiveness of production of consistent herbal formulations. To meet with these challenges will involve interdisciplinary coordination among the pharmacologists, botanists, ethnopharmacologists and clinical researchers [8].

This review is intended to give a timely description of *Momordica dioica* with a focus on its phytochemical components, conventional medicinal applications, and novel finding about its neuroprotective effects. Further, the review attempts to draw conclusions regarding the mechanism of action and summarize experimental data and identify gaps in available knowledge that should be investigated. This article will attempt to blend the traditional and scientific evidence available on *M. dioica* with the view to highlighting its therapeutic value and encouraging future use in neuropathy prevention and treatment. The antioxidant, anti-inflammatory and neuronal stabilizing benefits of the plant bring new horizons on the usage of natural products as countermeasure against neurodegeneration. With the increase in incidences of neurological disorders worldwide and more so in the aging population, the discovery of safe, effective and affordable neuroprotective compounds using medicinal plants, such as *M. dioica*, becomes more topical. Clinical validation, molecular pharmacology and development of formulation studies are uniquely necessary to achieve the therapeutic potential of this unused but pharmacologically diverse plant species [9].

II. BOTANICAL DESCRIPTION

2.1. Taxonomy and Classification

Momordica dioica Roxb. ex Willd. belongs to an important family Cucurbitaceae also referred as gourd or cucumber family. It has more than 900 species that are spread around the world and are economically and medically valuable. A genus is called Momordica comprising around 60 species, of which *M. charantia* and *M. dioica* are popular due to their pharmacological use [10]. The taxonomic hierarchy of Momordica dioica is the following one:

- **Kingdom:** Plantae
- **Subkingdom:** Tracheobionta (vascular plants)
- **Division:** Magnoliophyta (angiosperms)
- **Class:** Magnoliopsida (dicotyledons)
- **Order:** Cucurbitales
- **Family:** Cucurbitaceae
- **Genus:** *Momordica*
- **Species:** *Momordica dioica* Roxb. ex Willd.

This type is dioecious where male and female flowers grow on different plants, so there must be cross-pollination to make fruit. Momordica genus is named because it means to bite in Latin and it is possible that the jagged edges of the leaves are what has made it take its name, and the species epithet which is dioica indicates that the plant is dioecious in nature [11].

2.2. Morphological Features

The plant is very uniquely shaped such that it stands out very easily among other plants that belong to the Cucurbitaceae family. It is a climbing perennial herbaceous plant having tendrils and tuberous roots. The leaves, flowers, fruits and roots that constitute its structure are also essential in identification but also serve as medicine.

Fig.1: *Momordica dioica* Roxb.

2.2.1. Leaves

M. dioica has simple, alternate, palmately lobed leaves, and conveys a common number of 5-7 lobes. They are of medium sized appearance with a bumpy texture and jagged edges. The leaves are rough as the surface has fine trichomes. The leaves are deep green in color, and as the plant matures, its color becomes darker. These are carried on thin petioles and exhibit peltate foundation. They are phytochemically rich, particularly in polyphenolic compounds and flavonoids and hence their medicinal use in inflammatory and oxidative stress related disorders [12].

2.2.2. Tendrils

Being a climbing plant, M. dioica forms axillary, unbranched tendrils that help it to hug the plant as it grows along the support upward. The tendrils are susceptible to touch, and curl about adjacent objects, a characteristic of numerous cucurbits.

2.2.3. Flowers

It is a dioecious plant, which forms unisexual flowers on male and female plants. Both the flowers are solitary, axillary and supported on slender peduncles. The male flower has five free and a fused corolla tube. They bear three stamens of which two are adherent leaving one of them free. Anthers are oblong shaped and yellow. The ovary in female flower is inferior, style and stigma are three lobed. They are usually bigger than male flowers and when they are pollinated fertilically they produce fruit. These flowers are yellow whose bloom is normally during the monsoon period. Pollination is mostly entomophilous and insects like bees help in the process [13].

2.2.4. Fruits

The most commonly consumed part of M. dioica is the fruit, which is equally important both in culinary and medicine value. It is a small elongated, ovoid to ellipsoid berry which measures 4-8 cm in length. The texture is like bristly, spiny property because of the firm spines whose tips are soft and fleshy-like--thus the name, spiny gourd. The unripe fruits are green and gradually become orange-red, when ripe. The fruit has many seeds implanted in the fleshy pulp. The seeds are flattened, ovoid and brown-black. The pulp and seeds are low in nutritional value with a wide range of bioactive substances like flavonoids and triterpenoids, which explains their pharmacological use [14].

2.2.5. Roots

It has a tuberous, perennial root system that makes the plant to grow back again every year without seeds. The roots consist of cylindrical, fleshy with brown outer cover and creamy white on the inside. Root extracts are traditionally applied in different kinds of indigenous systems of medicine in order to treat reproductive disorders, fever, and general debility. Phytochemical analysis of roots shows the existence of alkaloids, saponins as well as steroids, which are associated with their effectiveness in treatment [15].

2.3. Geographic Distribution and Habitat

Momordica dioica originates in the Indian subcontinent and it has a special affinity to tropical and subtropical environments. The plant is common in India, Nepal, Bangladesh, Sri Lanka, Myanmar and some regions of Southeast Asia. Sporadically, it also occurs in East Africa and right in South Pacific where also similar climatic conditions prevail. The plant is widely grown or occurs wild in states of West Bengal, Jharkhand, Odisha, Bihar, Maharashtra, Madhya Pradesh, Gujarat, Uttar Pradesh and Assam in India. It is usually found in forest edges as well as farms, hedge rows and wastelands [16]. The wild varieties can be discovered in shaded areas especially near to streamlets or fallow lands which shows that they are adaptable in humid environment especially where the soil is moist. It prefers well-drained soil of loamy and sandy texture of good organic content. Even though the plant is relatively tolerant to partial shade, it grows well in light spots with ample sunlight and moderated rainfall. It reaches altitude as high as 1,200 meters above sea level, but the fruit quality and yield is best on the low-lying plains. Its growth cycle depends on such environment factors as temperature, humidity, and photoperiod. The plant is very seasonal and the initiation of its growth seems to happen in early monsoon (June July) and fruiting continues throughout late monsoon and early autumn.

2.4. Cultivation and Harvesting Practices

Momordica dioica has long been used as medicinal and nutritive crop and there is increased interest to commercially propagate this crop because of its commercial value and therapeutic application. Nevertheless, its successful cultivation poses some kind of agronomic difficulties mainly due to its dioecious nature and unfavorable rate of seed germination. As a result, vegetative propagation is the best alternative usually using healthy root tubers or vine cuttings to attain genetic uniformity and increased establishment. Rice is planted during the onset of the monsoon (June to July) due to an ideal mixture of moisture and temperature in the soil to nourish the growth. Deep, evenly drained fertile loamy soils are suitable to cultivation and the addition of organic manures (compost or farmyard manure) to improve soil fertility is very beneficial. Since it has a climbing growth habit *M. dioica* needs to be trained on the trellis or support system like bamboo stakes or wire mesh so that it can grow taller to make harvesting of fruits easier and reduce the occurrence of the diseases. The plants should be adequately spaced (usually 1.5 to 2 meters apart) and the ratio of male to female plants should be balanced (usually 1:10). This is done to provide very good pollination and to set well [17].

Moderate irrigation that is well controlled is advised especially on dry periods to prevent water logging and root rot. They can be preserved by regular weeding and mulching that serve to maintain soil moisture and inhibit weeds. The plant is quite strong however it is sometimes affected by fungal infections including powdery mildew and downy mildew

which can be conveniently treated by organic fungicides or preparation of neems. The maturity of the fruits occurs in 45-60 days of the planting period and it is done manually with regular means after the fruits gain the marketable size. The immature and green fruits are used in cooking and to perform therapeutic purposes because it has the best nutrient and phytochemical profile. After harvest, care of the fruits (to avoid bruising and spoilage) should be taken and they are optimally stored under cool and shaded conditions. In the medicinal preparation of the plants, various parts of the plants like the roots, leaves, etc. are sometimes collected, washed and dried in shade before other processing. In general, the traditional knowledge of cultivation combined with modern agronomic methods can enhance the productivity, quality and pharmacological potential of *Momordica dioica* to an enormous degree [18].

III. TRADITIONAL AND ETHNOMEDICINAL USES

In South and Southeast Asia, traditional medicine has traditionally known the medicinal potentials of *Momordica dioica* Roxb. ex Willd. a plant that has been used widely in its broad-spectrum medicinal value. *M. dioica* has a long history of being used in different indigenous healing systems such as the Ayurveda, Unani and Siddha systems to treat a broad spectrum of illnesses, covering digestive disorders, gynecological conditions, inflammation and metabolic disorders. The plant has good reputation in the rural and tribal communities of India, Nepal and Bangladesh where almost all its parts roots, leaves, fruits and seeds are used in the form of a medicine. Such applications are usually grounded on empirical knowledge that is passed over through the generations and remain important in the primary healthcare, particularly in underserved regions [19].

In the context of its traditional uses, it has been noted to have been used in the treatment of gastrointestinal disorders as one of the most common reports related to it. Root or leaf decoction is employed in the treatment of dysentery, diarrhea, intestinal worms and flatulence. Plant is supposed to work as a mild laxative and some digestive stimulant, contributing to the smooth operation of the gastrointestinal tract. Its fruit, especially when unripe, is a very popular vegetable, and is reputed to be carminative and tonic. Tribal medicine mostly advises people to consume the fruit as a remedy to appetite and invalid remedy on biliousness and acidity.

A number of ethnobotanical studies have cited fruit and leaf preparations in the treatment of diabetes mellitus. The juice or aqueous extracts of the fruit are used to help balance sugar levels and in most instances it is administered on an empty stomach especially in some rural communities. Although most of these practices were regarded as anecdotal, new pharmacological efficacies have been upholding historical usage as evidence of substantial antidiabetic and insulin-mimetic efficacies within preclinical approaches [20].

Ethnomedicine the use of *M. dioica* is also common in the field of reproductive health. Root and seeds preparations In several tribal structures, there is use of root and seed preparations in treating infertile couples, menstrual irregularities, and postpartum complications. The plant has a reputation of being an aphrodisiac especially when the root is taken with milk or other herbaceous additives. Traditionally in women it is used to maintain the health of the uterus, so as well as to boost fertility, and in men it is taken to increase sexual vigor and manage erectile dysfunction. There are also the communities where terms of birth control or preventing miscarriage are used, but such activities still need more clinical confirmation because the amount of dosage is not standardized [21].

The analgesic/anti inflammatory capacity of *M. dioica* has rendered it a household name in the treatment of local pains and chronic inflammatory ailments. Seeds are crushed and the extracted paste is used together with root paste in poultices which can be applied topically to relieve pain and swelling of the joints and be utilized in relieving insect bites. The boiled root in parts is applied to abscesses and wounds to encourage the healing progress and lessen the contamination, implying that the plant has anti microbial and wound healing actions. In topical applications these are especially common in Ayurvedic and folk medicine where the plant would be categorized as tikta (bitter) and the rasa as katu (pungent) and would be having ushna virya (being hot in effect) and thus appropriate where excess kapha and vata dosha is considered [22].

In respiratory conditions, the decoction of the leaves or fruit is applied in the ailments such as asthma, bronchitis and chronic cough. The herb is supposed to have expectorant effects, and so it is useful in removal of mucus within the respiratory system. Furthermore, other herbs are occasionally added to *M. dioica* complementing it to enhance its effectiveness in the case of respiratory infections; tulsi (*Ocimum sanctum*) or black pepper (*Piper nigrum*).

Traditionally hepatoprotective effects and detoxifying properties of *M. dioica* are also recognized. The plant is used in support of liver action in a number of ethnomedicinal practices, particularly with sufferers of jaundice or drug-damaged liver tissue. The harsh flavor of the fruit and leaves is said to demonstrate their purity qualities and blood cleansing purposes. Moreover, the plant is used as a general health tonic. It is said to boost immunity and give tissues a facelift through its rich antioxidant levels. During monsoon in most parts, the young fruits are taken every day to boost immunity in the body to counter the sickness that comes with this rainy season. The external application of *M. dioica* extract has also been used in skin care mainly in the treatment of rashes, eczema and fungal infections besides these outside uses. This is due to antimicrobial activity exhibited by the plant, which makes it applicable in the treatment of dermal infections particularly in combination with other herbal components [23].

Nutritionally, *M. dioica* fruits contain all the important nutrients including vitamin A and C, iron, calcium, and dietary fiber. This combination of food and medicine makes the plant a functional food (or nutraceutical), one which undermines the distinctions between diet and treatment in folk medicine. The popularity of using *M. dioica* across the Indian subcontinent supports the importance of this plant in local and traditional diets, food cultures and even traditional health systems using extensive plant-based interventions.

Though there is wide traditional application of these ethnomedicinal claims, there is no scientific verification of the same. Although many of its biological actions including antioxidant, anti-inflammatory, antimicrobial and antidiabetic activity have been validated by several *in vitro* and in vivo studies, most of the traditional uses, particularly in the female reproductive system and neurology, have to be subjected to strict clinical testing. Dosage standardization, active component identification, and elucidation of pharmacodynamic mechanisms are among the needed measures of *M. dioica* incorporation into evidence-based phytotherapies [24].

Accordingly, it can be concluded that *Momordica dioica* is a typical example of such a medicinal plant the ethnomedicinal value of which has been very rich and diverse. Its application in the traditional healthcare system in treating digestive, metabolic, reproductive, respiratory, hepatic, and inflammatory disorders shows the breadth to be used in treating diseases. The fact that the plant has been accepted in both cultural and medicinal fields as well the initial pharmacological backing offers a good argument of more research and development. Converging traditional and modern sciences will not only establish legitimacy of these practices but will also establish by new botanical drugs against chronic and lifestyle related disorders including neurodegenerative diseases.

IV. PHYTOCHEMISTRY OF *MOMORDICA DIOICA*

4.1 Major Phytoconstituents

Momordica dioica Roxb. ex Willd. is a common herb in traditional medicine and is an attraction in modern pharmacology due to the abundance of phytochemistry. Its chemical components are also indispensable towards explaining its pharmacodynamic effects and therapeutic properties which include civilizing, its antioxidant, anti-inflammatory, antidiabetic, hepatoprotective, and neuroprotective properties. Phytochemical profile of *M. dioica* is quite diverse and consists of different types of bioactive secondary metabolites such as flavonoids, triterpenoids, saponins, alkaloids, phenolics, steroids, glycosides and essential nutrients. The distribution of these compounds throughout the plant varies in parts of the leaves, roots, fruits, and seeds and acts synergistically leading to the multifaceted biological effect of the plant [25].

4.1.1 Flavonoids

Phytochemicals found in *M. dioica* include flavonoids, which comprise one of the most pharmacologically significant categories. Such polyphenolic compounds are also known by their high antioxidant potential, which is provided by free radical scavenging, iron sequestration, silver and any other agent that might cause oxidation and also the manipulation of antioxidant enzyme systems. Some of the major flavonoids found in the *M. dioica* are quercetin, kaempferol, apigenin, and their glycosides. The presence of such compounds is largely in the leaves and fruits and they mediate the various biological mechanisms such as those of inflammation, oxidative stress, and neurodegeneration. These two compounds quercetin and kaempferol specifically have been vividly researched in regard to their neuroprotective effect. They prevent generation of pro-inflammatory factors, including TNF-alpha, IL-1 beta, and nitric oxide, and at the same time they increase the cellular antioxidant defense system by increasing the activity of such enzymes as superoxide dismutase, catalase and glutathione peroxidase. *M. dioica* has such flavonoids, which indicate its ability to reduce oxidative stress and their neuronal damage [26].

4.1.2 Triterpenoids

The other important class of phytoconstituents isolated out of *M. dioica* belong to the family of triterpenoids, especially those extracted out of the roots and fruit rind. They are anti-inflammatory, hepatoprotective and adaptogenic compounds. Notable triterpenoids that have been reported of include ursolic acid, oleanolic acid and lupeol. The compounds have shown strong anti inflammatory effects by upregulating the Nuclear factor kappa B (NF-kB) signaling pathway that is critical in regulation of inflammation and apoptosis in the neurological and systemic diseases. Modulation of Mitochondrial integrity and shield against excitotoxicity in neuronal cells have also been shown by Ursolic acid and Oleanolic acid. They have raised interest in using them to prevent and treat neuro degenerative diseases like Alzheimer and Parkinson due to their efficiency in preventing and improving mitochondrial biogenesis and lipid peroxidation [27].

4.1.3 Saponins

The saponins are glycosidic compounds with the feature of being surfactants and they are in abundant in the seeds and roots of *M. dioica*. Such bioactives have proven various pharmacological activities embodying hypoglycemic, antimicrobial and anti-inflammatory characteristics. In structure, they are made up of a hydrophobic aglycone (sapogenin) and hydrophilic sugar moiety, which gives it a special pharmacokinetic character. Saponins are mentioned in the context of neuroprotection to regulate neurotransmitter balance and inhibit inflammatory cascades and thus affecting the central

nervous system [28]. There is preliminary evidence that the saponins of *M. dioica* could help in reducing neuroinflammation and in preventing apoptosis of neuronal cells; which would require extensive research to isolate and identify individual saponins that confer the same.

4.1.4 Alkaloids

Alkaloids have a lower concentration than flavonoids and triterpenoids in the *M. dioica* but play an important role in its pharmacology. They are mainly present in the roots and the seeds and are heterocyclic compounds containing nitrogen. Other alkaloids were found like momordicine and momordicinin which is thought to be analgesic, sedative and anticonvulsant. The activity of these compounds is neuroprotective in its multiple forms, containing inhibition of monoamine oxidase (MAO) enzymes, modulation of calcium channels, as well as suppressing the neuroinflammatory mediators. The presence of neuroactive alkaloids has made them prospective candidates waiting to be explored further on the application or use of alkaloids in central nervous system (CNS) related disorders [29].

4.1.5 Phenolic Compounds

M. dioica leaves and fruits have been found to contain phenolic acids: ferulic acid, gallic acid, chlorogenic acid, and caffeic acid. Well-known antioxidant properties of these compounds are attributable to reactive oxygen species (ROS) neutralization ability by their hydroxyls, thus preventing an oxidative stress-induced cellular ailment. The mechanism of phenolic compounds on defining the characteristics of the inflammatory signal, as well as on the regulation of the process of neuronal apoptosis, also belongs to the research. The fact that they work synergistically with flavonoids and other polyphenols makes them have a strong antioxidative, and neuroprotective activity in the plant in question. The compounds have been found helpful in enhancing the vascular health, and potentially positively affecting cerebral blood, an aspect that is very critical in averting neuronal damage that occurs due to ischemia [30].

4.1.6 Steroids

Steroidal compounds especially containing a β-sitosterol have been extracted in the seeds and roots of *M. dioica* and have shown various pharmacological outcomes such as anti-inflammatory, immunomodulatory and neuroprotective effects. β-Sitosterol has been found as a phytosterol that structurally is related to cholesterol that has been reported to be effective in experimental models of neurodegeneration by increasing cognitive performance of neurodegeneration by influencing synaptic transmission and preserving neurons. It also suppresses the activation of microglia and lowers neuroinflammation as a core aspect of the Alzheimer disease pathophysiology and other CNS conditions.

4.1.7 Glycosides

In *M. dioica*, glycosides are mainly extracted on the root and fruit fraction. These are cucurbitane-type triterpenoid glycoside which are typical of the Cucurbitaceae family. The compounds are involved in glucose metabolism regulation, cardiovascular health maintenance, and the cytoprotective responses. Whilst relatively little is known specifically about their neuroprotective effect, glycosides are known in general to be active in the central nervous system, through the modulation of enzyme activity and signal transduction pathways in cells. This fact, which is manifested by their presence in *M. dioica*, increases the pharmacological potential of the plant, particularly when this product is regarded together with other classes of bioactive elements [31].

4.1.8 Essential Nutrients and Trace Elements

Along with the secondary metabolites, the plant also contains important micronutrients, e.g., vitamin A (beta-carotene), vitamin C, iron, zinc, calcium, and magnesium, which are mainly located in the fruit. These are micronutrients that are important to the health and workings of the neurons. Both vitamin C and beta-carotene are antioxidants whilst minerals such as zinc and magnesium are co-factors of enzymatic reactions in the brain. These nutrients make the plant have an increased neuroprotective profile making it to be classified as a nutraceutical.

4.1.9 Volatile and Aromatic Compounds

The volatile compounds and essential oils of *M. dioica* have not been as thoroughly investigated, but initial analysis using GC-MS showed that terpenes, aldehydes and esters were present. These are aromatic compounds which can cause the antimicrobial and anti-inflammatory qualities in the plant and frequently the distinctive odor of a plant. Although how they contribute to neuroprotection remains unknown, they may end up working synergistically with other phytochemicals, contributing to the therapeutic profile of the plant [32].

V. PHARMACOLOGICAL ACTIVITIES OF *MOMORDICA DIOICA*

Momordica dioica Roxb. ex Willd, which is of tremendous therapeutic use in the traditional systems of medicine, has received much pharmacological exploration over the past few years. The extensive bioactivities of various preclinical research studies have been supported by its rich reservoir of phytoconstituents; flavonoids, triterpenoids, saponins, alkaloids, phenolic acids, glycosides, among others. These bio active materials act synergistically to produce numerous pharmacological effects. Among the most notable ones are antioxidant, anti-inflammatory, and and usage, antidiabetic agents, antimicrobial and hepatoprotective ones. These properties not only confirm conventional reports, but also, the *M. dioica* could be put forward as a potential drug discovery and phytotherapeutic agent [33].

5.1 Antioxidant Activity

Oxidative stress, a pathologic situation in which reactive oxygen species (ROS) and reactive nitrogen species (RNS) are produced abundantly, is a key to the development of different chronic diseases, which involve neurodegenerative diseases, diabetes, vascular diseases, and cancer. The antioxidant defense system plays an important role in asymptomatic disadvantaged species neutralization and redox homeostasis. The potent antioxidant property is also being established in plants that are abundant in phenolic and flavonoid compounds, including *Momordica dioica*. Several works have proved that extracts prepared using various parts of *M. dioica* especially its fruits and leaves have quite substantial free radical scavenging activity. The antioxidant power of the plant has also been established by standard in vitro assays including DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging, ABTS (2,2- azino-bis (3-ethylbenzothazoline, 6-sulphonic acid)) decolorization, ferric reducing antioxidant power (FRAP), and nitric oxide (NO) scavenging assays. The activity of ethanolic and methanolic extracts is usually greater than that of aqueous extracts implying involvement of alcohol soluble phenolics and flavonoids as the important compounds. The ROS-neutralising potency of flavonoids, e.g. quercetin and kaempferol, as well as phenolic acids, e.g. gallic acid and ferulic acid can be described as well-documented. They include the actions of these compounds to donate electrons or hydrogen atoms to neutralize free radicals, chelation metal ions in the production of ROS, and amplify endogenous antioxidant enzyme systems such as superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). *In vivo* preparation in animal models has demonstrated that intravenous application of M. dioica extracts exert considerable increases in antioxidant viability and decreases in indicators of lipid peroxidation such as malondialdehyde (MDA) signifying a general protection of the antioxidants. This activity is of special interest to the context of neurodegeneration and metabolic disorders when the oxidative stress is known as a leading etiological factor. The robust antioxidative properties of *M. dioica* may confirm the common usage of this plant as a general tonic agent and possible use in the prevention of chronic diseases associated with oxidative type of the damage [34].

5.2 Anti-inflammatory Activity

Inflammation is the body physiologic response to injury or infection but chronic unregulated inflammation is the basis of many pathological diseases such as arthritis, neurodegenerative diseases, cancer and cardiovascular diseases. Plants with the ability to inhibit inflammatory processes are very important in development of a safer and long-term treatment of anti-inflammatory conditions. Anti-inflammatory potential of *Momordica dioica* was consistently revealed in research; various extracts have proven to be effective both in vitro and vivo models of inflammation. Methanolic extracts of the fruit and stands have been documented to extensively suppress carrageenan induced paw oedema and cotton pellet induced granuloma in rats which are generally used as standard models of acute and chronic inflammation respectively [35].

The proposed anti-inflammatory effects of *M. dioica* can mainly be engaged to its effectiveness in shutting down pro-inflammatory signators like prostaglandins, leukotrienes, nitric oxide (NO), and pro-inflammatory cytokines like tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL-6) and interleukin-1 beta (IL-1 beta). The mechanisms of action rely on the down-regulation of major signaling pathways of inflammation, in particular, on nuclear factor-kappa B (NF-kB) and mitogen-activated protein kinase (MAPK). These pathways control the expression of the inflammatory enzymes, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) that are markedly inhibited by the addition of extracts of M. dioica. Use as a topical application of leaf paste or root decoctions has traditionally been used to treat swelling, pain and joint stiffness, and this corresponds to the systemic anti-inflammatory observed during pharmacological studies. The ability of this plant in modulation of both acute and chronic inflammation makes it ethnopharmacologically useful in its management of rheumatic disorders and more so; its potential value as a phytotherapeutic agent in the management of inflammatory disorders [36].

5.3 Antidiabetic Activity

Diabetes mellitus, especially type 2 diabetes, is a metabolic disorder, which is exemplified by persistent hyperglycemia as a phenomenon of insulin resistance or impaired secretion. Traditional antidiabetic drugs are known to elicit side effects accompanied by low long-term effectiveness; thus, alternatives based on plants are being sought. *M. dioica* has a historical fame as an antidiabetic medicine. Its fruits and leaves are often used in decocations and fruit juices to control the level of blood sugar and this has been approved both in vitro and in vivo. diabetes-induced animal studies using alloxan or streptozotocin (STZ) have proved that the use of *M. dioica* extracts greatly lower levels of fasting blood glucose, enhance glucose tolerance, and obtain insulin sensitivity [37].

This hypoglycemic activity of *M. dioica* is presumably acted via several mechanisms. Plant flavonoids and saponins were found to have beneficial impact on pancreatic beta-cell proliferation, were shown to stimulate insulin release, as well as increase peripheral uptake of glucose. The plant is also found to have inhibitory effects on carbohydrate-digesting enzymes 4-α-amylase and 4-amylosidase which delays the absorption of glucose in the intestine and postprandial blood glucose surges. Further, *M. dioica* has protective action on the pancreatic tissue and improves oxidative stress markers in diabetic animals. These results are not only a confirmation of its traditional use, but also indicate that the plant has the potential of a multi-targeted antidiabetic agent that can be used as a chronic therapy [38].

5.4 Antimicrobial Activity

Momordica dioica is traditionally used to treat skin infection, gastrointestinal disorders, and respiratory tract diseases due to the antimicrobial effects. These chemicals such as phenolic compounds, alkaloids and terpenoids give the plant an action spectrum against numerous bacterial and fungal pathogens by providing it with natural broad spectrum antimicrobial activity. The in vitro disc-diffusion and broth-dilution tests have been observed to demonstrate that Ethanolic and Methanolic extracts of *M. dioica* had pronounced inhibition effects against Gram-positive bacteria like Staphylococcus aureus and *Bacillus subtilis* and Gram-negative species like Escherichia coli, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. There is also antifungal effect against fever species such as *Candida albicans* and *Aspergillus niger*[39].

It is believed that the antimicrobial effect operates mechanistically by causing disruption to the microbial cell membranes, inhibition of nucleic acids synthesis and obstructing of their enzymatic processes vital in microbial growth and reproduction. In particular, triterpenoids and saponins are at risk of compromising cell wall integrity and causing cell lysis. *M. dioica* dried leaf extracts or paste applied directly on the wound or skin eruption surface is traditionally used in the standard practice of wound healing, boils and skin eruptions, and scientific studies affirm this. Moreover, the antibacterial property of the plant has the potential of treating antibiotic resistance by delivering alternative medicine or supplementary treatments [40].

5.5 Hepatoprotective Activity

The liver, which plays a pivot role in metabolism and detoxification of toxins, drugs, infections and oxidative stress, is very susceptible to toxicity. Hepatoprotective agents are essentially used to promote liver function and further avoid the development of chronic liver diseases. Popular application of the *M. dioica* on treatment of jaundice and liver diseases has compelled its scientific exploration on hepatoprotection. Effect of M. dioica extracts has been shown to cause significant reduction in serum concentration of hepatic enzymes including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin through experimental examination on the animal models of liver injury based on carbon tetrachloride (CCl_4), paracetamol or ethanol instigation. These indicators represent the harmful damage to hepatocellular and their reduction represents hepatic protection and functional restoration [41].

Histopathologic analysis of liver tissues of animals treated indicates the maintenance of hepatic structure, loss in necrosis as well as inflammatory congestion. Such protective actions are due to the antioxidant and the antiinflammatory effects of the flavonoids, saponins and phenolic compounds found in the plant. More specifically, the constituents suppress oxidative reactions in the stress condition by scavenging free radicals, suppress detoxification enzyme activity, and stabilize hepatocyte membranes. Hepatoprotective effect of *M. dioica* justifies its use in polyherbal liver tonics and also of an interest of using it as a lead compound in formulating herbal recipes to treat her liver diseases, particularly induced by chemical injuries and oxidative stress [42].

VI. NEUROPROTECTIVE ACTIVITY OF *MOMORDICA DIOICA*

Neurodegenerative diseases, including Alzheimer disease (AD), Parkinson disease (PD), Huntington disease and other diseases, which lead to starts of the mind, are a major health burden throughout the world with no curative solution. Pathophysiology of the disorders is defined as progressive neuronal structural and functional loss, caused, mainly, by oxidative stress, neuroinflammation, mitochondrial dysfunction, excitotoxicity, and protein misfolding. The plant-based products and compounds have become prospects of therapeutic application in reducing neurodegeneration over the last 20 years thanks to their multi-targeted nature, safety, and their use in traditional medicines.

Momordica dioica Roxb. ex Willd. (Cucurbitaceae) has been cited in ethnomedicine not only because of the anti-inflammatory and antidiabetic properties but also because it successfully treats nervous system revitalization, as well as age-related conditions. Support of these traditional claims is emerging in the certain pharmacological data that have shown the neuroprotective efficacy of *M. dioica*, which is mainly linked to its antioxidative, anti-inflammatory and neuroregulatory effects [43].

6.1 Mechanisms of Neuroprotection

6.1.1 Antioxidant Defense and Free Radical Scavenging

Among the most important neuroprotective effects of *M. dioica*, the influence on the oxidant system is to be distinguished. The brain is especially vulnerable to lipid-peroxidative damage because of its content of lipid and its great requirement of oxygen. When not balanced by antioxidants, reactive oxygen species (ROS) cause lipid peroxidation, damage of DNA, and disruption of mitochondrial functions, all of which cause cell death in neurons. Several articles have shown *M. dioica* (particularly, the methanolic and ethanolic extract of its fruits and leaves) to have a high free radical scavenging capacity in vitro, such as DPPH, superoxide radical and hydroxyl radical assays. All this is due to a large amount of flavonoids (e.g., quercetin, kaempferol), phenolic acids (e.g., gallic acid, ferulic acid), and saponins, which are able to counteract ROS, stimulating the expression of endogenous antioxidant enzymes (e.g. superoxide dismutase, catalase and glutathione peroxidase) and inhibiting markers of lipid peroxidation such as malondialdehyde (MDA). These characteristics play an imperative role in neuronal stability and performance [44].

6.1.2 Anti-inflammatory Action in Neural Tissues

A typical characteristic of neurodegenerative diseases is chronic neuroinflammation and the occurrence of a persistent activation of microglia and the secretion of pro-inflammatory cytokines (TNF-alpha, IL-1beta, and IL-6). The constituents in M. dioica have been exhibited to have a big effect of anti-inflammatory both as in vitro and in vivo trial. The anti-neuroinflammatory affectors identified as the triterpenoids, ursolic acid and lupeol, and the flavonoids such as apigenin are effective in halting the neuroinflammation cascades by suppressing the development of key transcription factors, including NF-KK and MAPKs. These compounds regulate the expression of inducible nitric oxide synthase (iNOS) and COX-2 that is related to inflammatory neurotoxicity. M. dioica can support viability of the neurons by blunting the liberation of inflammatory mediators, and thus it does not spread neuroinflammatory injury [45].

6.1.3 Cholinesterase Inhibition and Cognitive Enhancement

The other neuroprotective mechanism remains the modulation of cholinergic signaling that is also extremely important in learning and memory processes. There is a close connection between dementia-Alzheimer and the decreased rate of acetylcholine caused by hyper-activity of acetylcholinesterase (AChE). AChE inhibitors are therefore much sought after like natural ones in the management of AD. It was preliminarily reported that M. dioica increases availability of acetylcholine in the synapse by being an acetylcholinesterase inhibitor and thus, facilitating cholinergic neurotransmission. This could help in enhancing memory maintenance and the ability to learn as has been seen to be the case with some rodent models after oral insinuation of M. dioica extracts. This property runs with advantage the plant to be useful as functional ingredient in the management of cognitive impairment notwithstanding the fact that there is need of further detailed neurobehavioral studies.

VII. CONCLUSION

Momordica dioica Roxb. ex Willd., a family of medicinally significant plant in Cucurbitaceae has enormous pharmacological and ethnomedicinal significance. Commonly found in conventional South Asian medicine, it has been appreciated due to its medicinal values in the treatment of gastrointestinal disorders, diabetes, inflammatory conditions, liver diseases and reproductive disorders with limited side effects. These traditional assertions have been confirmed in modern phytochemical studies that have demonstrated a wide range of bioactive components such as flavonoids, triterpenoids, phenolics, alkaloids, saponins as well as sterols, many of which have potent anti-oxidant, anti-inflammatory, anti-diabetic, antibacterial and liver protecting activities. The most curious of them all is the recent data around the neuroprotective nature of M. dioica. The plant can be useful in the prevention and treatment of neurodegeneration processes like Alzheimer and Parkinson diseases due to its capabilities to rudiment oxidative stress and impair neuroinflammation, cytokines, and neurotransmitters, and cholinergic activity. The phytochemical synergy which works on various molecular pathways leading to neuron degradation and cognitive deterioration is credited to be the major effects of this substance. Although pharmacological evidence of *M. dioica* is encouraging, there are deficient clinical data. Consequently, the next steps should be geared towards isolating bioactive compounds, mechanism based research, pharmacokinetics profiling of such compounds and test-tube human studies to prove therapeutic efficacy and safety. Development of plant materials, as well, into effective phytotherapeutics or nutraceuticals will rely on standardization and quality control of plant material. Conclusively, *Momordica dioica* is a pharmacologically diverse herb that has a lot of potential in integrative medicine particularly in the treating oxidative- and inflammation-based chronic diseases. Its cerebral benefits classify it as an appealing natural resource to the production of brain health supplements and herb-based neurotherapeutics. The interplay between contemporary science and the ancient knowledge about the plant remains an indication of the importance of the plant in drug development and integrative medicine.

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