



A MINI REVIEW ON CUCUMBER & GILOE: A NEUROPROTECTIVE & IMMUNOMODULATOR AGENT

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Abstract

In the present scenario chemicals compounds are failed to show a clinically relevant effects as Neuroprotective and immunomodulator. The uses of phytochemicals are supportive boon for our health systems against enhancement of side effects. There are various dietary supplements which possess immunomodulatory and neuroprotective property. Alzheimer's occurs due to the collection of beta amyloid proteins in the brain which damage the organ and impact cognitive function of brain. Single drug and nutrient-based interventions have failed to show a clinically relevant effect on Alzheimer's disease. This has led to the need for research into treatments, that approaches the condition in entirely different way. Cucumber cerebrosides possess neuroprotective effects against A β protein, which may be a potential nutritional preventive strategy for neurodegenerative diseases with little or no side effects. This article represents the review on Cucumber for management of Alzheimer Disease as well as immunomodulatory activities of giloy.

Key words: Alzheimer, A β protein, Cucumber, Fisetin, Immunomodulator, Giloy

Introduction

Natural product is a substance produced by a living organism which is found in nature. Natural products are complex compounds that possess diverse activity. Several species have been screened that can have significant biological activities & potential for drug development. These compounds interact with their target molecule to produce beneficial effects for the treatment of various diseases. These efforts have yielded the isolation of number of drugs from bioactive compounds. Thus, Natural product presents many challenges to the structural and synthetic organic chemistry.

Cucumbers have long been used as food and traditional medicine in Asian countries. These Cucumbers are potential source of high value added compounds with therapeutic properties such as tri-terpene glycosides, Carotenoids, Bioactive peptides, Vitamins, Minerals, fatty acids, Amino acids. In the present time as per literature survey it is found that sea cucumbers have shown their medicinal value in which neuro-protective activity is one of them.

Alzheimer disease (AD):

It is a progressive neurodegenerative disease which

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leads to gradual degeneration of the human brain which is being dramatically increasing worldwide. It is a most common form of dementia. Dementia is a term used for progressive mental disorders which affects memory, thinking, comprehension and other essential brain functions. In the Alzheimer, memory loss is one of the earliest symptoms along with changes in personality or behavior. It is believed that Alzheimer's disease results due to increase of the production and accumulation of a specific protein which is called as beta-amyloid protein, found in the brain that leads to nerve cell death. It is characterized by aggregation of protein and tangles known as tau protein. Alois Alzheimer had discovered this disease in 1906 so it is named. Alzheimer has been estimated to account for 50%–60% cases of dementia commonly observed in old-age population. Globally about 25 million people are suffering from Alzheimer Disease. This number can increase up to 114 million by the year 2050.

The enzymes Cholinesterase such as acetylcholinesterase (AChE) and butyrylcholinesterase (BChE) are key enzymes that play important roles in cholinergic transmission by hydrolyzing the neurotransmitter acetylcholine. A number of scientific hypotheses are embracing the explanations of various mechanisms underlying Alzheimer Disease. The popularly

backing hypotheses are described below:

According to the Amyloid cascade Hypothesis, Deposition of A β protein in form of amyloid plaques in brain tissues, is the hallmark for neurodegeneration in Alzheimer Disease. An imbalance of A β production and disposal results in Alzheimer's disease includes formation of neurofibrillary tangles by tau proteins and plaques formation. The increased amount of plaque formation leads to synaptic dysfunction, memory impairments and brain damage⁵. A β (Amyloid beta protein) is generated by proteolytic cleavage of Amyloid precursor protein (APP) by β and α secretase enzymes. BACE₁, cleaves APP to form a membrane bound soluble C-terminal fragment, which gets subsequently cleaved by α -secretase enzyme to form A β -40 and A β -42.¹⁸

Cholinergic hypothesis is based on presynaptic deficits in brain of Alzheimer Disease patients. Cognitive dysfunctions are seen in Alzheimer's patients which is contributed by degeneration of cholinergic neurons in the brain, accompanied by loss of cholinergic neurotransmission in cerebral cortex part of brain. It has been observed in patient of Alzheimer's that activity of choline acetyltransferase and Acetylcholine esterase (AChE) are decreased. Failure in cholinergic system results in imperfections in learning and impairment in memory¹⁸.

The Glutamatergic hypothesis is based upon an abnormal alteration in GluN₂A containing N methyl-D-Aspartate receptor (NMDA) which results improper synaptic function leads to development of neurotoxicity through GluN₂B containing NMDA receptors¹⁹.

The δ hypothesis is based on the observation that δ dysfunction (abnormal levels, hyperphosphorylation, or ubiquitination), in the absence of amyloid pathology, is sufficient to cause synaptic and neuronal loss.

Despite enormous scientific efforts that are focused on the prevention of Alzheimer Disease, no pharmacotherapeutic agents are available either for prevention or treatment of Alzheimer Disease. There are five drugs namely Tacrine, Rivastigmine, Donepezil, Galantamine and memantine, approved by Food and Drug administration (FDA) in 2003 for Alzheimer Disease as first line drugs.

Except memantine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, the other four are choline esterase inhibitors. These drugs (reversible acetylcholinesterase inhibitors (AChEI) act through inhibition of AChE and butyrylcholinesterase (BChE). Tacrine is currently discontinued because of liver toxicity. it was the first FDA approved drug in 1993 while donepezil

was discovered in 1996, galantamine in 2004 and rivastigmine on 2006.⁸

The ageing process is deleterious for fitness, but can nonetheless evolve as a consequence of the declining force of natural selection at later ages, attributable to extrinsic hazards to survival, ageing can then occur as a side-effect of accumulation of mutations that lower fitness at later ages or of natural selection in favour of mutations that increase fitness of the young but at the cost of a higher subsequent rate of ageing. Once thought of as an inexorable, complex and lineage-specific process of accumulation of damage, ageing has turned out to be influenced by mechanisms that show strong evolutionary conservation.

Thus age-related disorders currently represent one of the most important and challenging health problems worldwide. Therefore, much attention has been directed towards the design and development of neuroprotective agents derived from natural sources. These phytochemicals have demonstrated high efficacy and low adverse effects in multiple in vitro and in vivo studies. Among these phytochemicals, dietary flavonoids are an important and common chemical class of bioactive products, found in several fruits and vegetables. Luteolin and Fiestin are an important flavone, which is found in several plant products, including broccoli, pepper, thyme and in cucumber. Numerous studies have shown that Fiestin possesses beneficial neuroprotective effects both in vitro and in vivo. That's why scientists have taken interest in flavonoid fisetin.

Immunomodulators:

Immunomodulators are substances that help to regulate and normalize the immune system. Immunomodulators are recommended for those people who having autoimmune diseases and are in chronic illness to restore immune system health in people who have been on lengthy courses of antibiotics or anti-viral therapies. Immunology is a broad branch of biomedical science that covers the study of all aspects of the immune system in all organisms. It deals with the physiological functioning of the immune system in states of both health and disease, malfunctions of the immune system in immunological disorders (autoimmune diseases, hypersensitivities, immune deficiency, allograft rejection); the physical, chemical and physiological characteristics of the components of the immune system in vitro, in situ, and in vivo.

An immune system is a collection of mechanisms within an organism that protects against disease by identifying and killing pathogens and tumor cells. It detects

a wide variety of agents, from viruses to parasitic worms and needs to distinguish them from the organism’s own healthy cells and tissues in order to function properly. Detection is complicated as pathogens adapt and evolve new ways to infect. The key primary lymphoid organs of the immune system are thymus and bone marrow while secondary lymphatic tissues such as spleen, tonsils, lymph nodes, adenoids and skin. To survive this challenge, several mechanisms are evolved that recognize and neutralize pathogens. Parts of the immune system are antigen-specific, systemic and have memory. Self/non-self-recognition is achieved by having every cell display a marker based on the Major Histocompatibility Complex

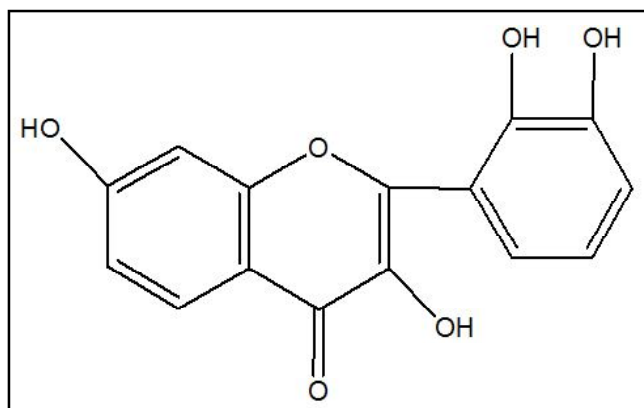
(MHC). Any cell not displaying this marker is treated as non-self and attacked.

Giloy is a widely used shrub in folk and ayurvedic systems of medicine. The chemical constituents of *T. cordifolia* belong to different classes that include alkaloids, steroids, glycosides, diterpenoid lactones, polysaccharides, aliphatic compounds, phenolics, and sesquiterpenoids. It is an evident from human history that medicinal plant have been treatment regimen to cure a variety of disease. In plant some chemicals are present which works same as conventional drug. These Plant study is known as ethnobotany for knowing medicinal value. It is a large, climbing shrub with several twining branches. Its leaves are simple, alternate, extipulate and having long petioles. Their Flowers are unisexual. Male flowers are clustered while female flowers are solitary. Their fruits are aggregate of 1-3 ovoid smooth drupeletes on thick stalk with sub terminal style scarlet orange coloured.

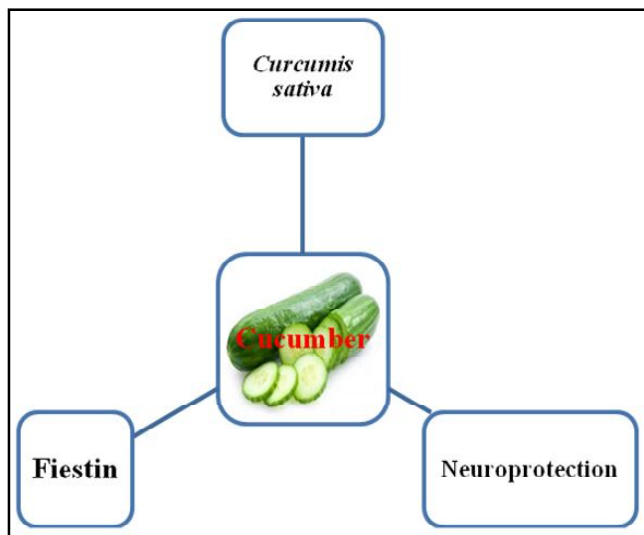
The ripened *T. cordifolia* barks are freshly collected, cut, dried in shade and then powdered coarsely. Then the powder is defatted with petroleum ether at temperature 60-80°C and extracted through soxhlet apparatus using hexane. The extract is dried under reduced pressure by rotary vacuum evaporator and the extract is then stored in refrigerator. *T. cordifolia* is expressed and recommended as a monoherbal as well as polyherbal preparation. Although it is alcoholic but the aqueous extracts have been verified positively for immuno-modulatory activity. This plant is distributed throughout the tropical region of India from Kumaon to asam and in north region extending through Bengal, Bihar and Kerala.

Giloe arrests AMA formation and reduces formation of this. It boosts natural immunity of body The term reverse pharmacology was being proposed by Vaidya to understand mechanism of action of herbal drugs at multiple level to optimize safety, efficacy and acceptability of the leads from natural product.⁹

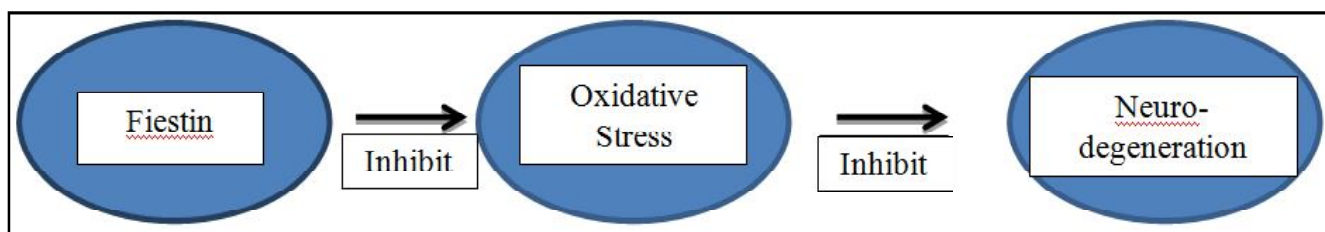
The water and ethanol extracts of stem of *T. cordifolia* inhibit immunosuppression produced by cyclophosphamide. The ethanol extract of stem of the plants inhibits cyclophosphamide-induced anemia. The

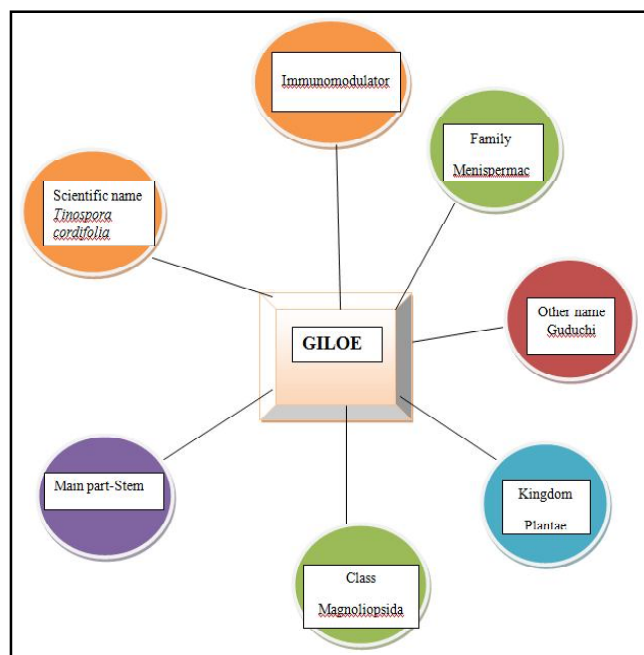


Fisetin



Cucumbers are a good source of fisetin. It is associated with protecting nerve cells, improving memory and decreasing the risk of Alzheimer’s in mice.¹





water extract of the plant is found to be more potent than the other extract. An arabinogalactan has been isolated from the dried stems of *T. cordifolia* and examined by methylation analysis, partial hydrolysis and carboxyl reduction. Purified polysaccharide showed polyclonal mitogenic activity against B-cells. Their proliferation did not require macrophages.

It appear that *T. cordifolia* improves the phagocytic function without effecting the humoral or cell mediated immune system. The activity of a crude extract formulation containing *T. cordifolia* and other plant drugs was evaluated in experimental amoebic liver abscess in golden hamsters and in immunomodulation studies. The formulation had a maximum cure rate of 73% at a dose of 800 mg/kg/day in hepatic amoebiasis reducing the average degree of infection to 1.3 as compared to 4.2 for sham-treated controls.⁹

In immunomodulation studies humoral immunity was enhanced. The T-cell counts remained unaffected but cell-mediated immune response was stimulated as observed in the leukocyte migration inhibition (LMI) tests. Syringin and Cardiol inhibit the immunohaemolysis of antibody. Humoral and cell-mediated immunity was also dose independently enhanced.

Conclusion

Natural products play a major role not only in Allopathic drug system as well in Homeopathic systems. In near future we should expect noble Immunomodulating and neuroprotective products reaching the market. More newer neuroprotective agents as well as

Immunomodulating agents should develop which are helpful in treating autoimmune diseases like Myasthenia gravis, multiple sclerosis and non-autoimmune inflammatory diseases like asthma, allergy etc. without any side effects. These studies helps to come out actual importance of screening which is necessary for examining potency of any drug of particular category.

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