REVIEW ARTICLE

Insights of *Pergularia daemia* in Neurodegenerative Conditions: An Overview

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ABSTRACT

As a growing cause of mortality and morbidity, neurodegenerative diseases (NDs) are becoming increasingly prevalent throughout the world, particularly among elderly people. The symptoms of Huntington's disease and Parkinson's disease (PD) are characterized by the loss of neurons and the degeneration of neurons. Neurodegenerative diseases are understood to have several causes, but their causes remain a mystery. It is important to note that there are many approved drug regimens for NDs, which can be used to treat symptoms but cannot heal the condition. It may be possible to utilize natural products to prevent and treat NDs in a very positive way. Several perennial herbs grow along Indian roadsides, including *Pergularia daemia* (Asclepiadaceae). Thespecies can be found widely in tropical and subtropical regions. Natural medicine has developed a significant interest in this plant species, which is rich in flavonoids, glycosides, tannins, and terpenoids. Several chronic diseases, including cancer, arthritis, diabetes, and neurodegenerative disorders, have been successfully treated with these secondary metabolites. Aside from this, they have notable pharmacological properties, including analgesic, anorectic, and antioxidant properties. This review provides a synthesis of existing knowledge regarding the anti-inflammatory and neuroprotective effects of *P. daemia*, emphasizing its potential as a natural medicine source.

Keywords: Neurodegenerative diseases, *Pergularia daemia***,** Phytoconstituents, Neuroprotective effects.

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INTRODUCTION

Several neurodegenerative conditions occur throughout the body, such as the central nervous system (CNS) and peripheral nervous system (PNS), which negatively impact millions of individuals around the world. As neural networks disintegrate, neurons die, and these terminally differentiated cells are unable to renew themselves effectively, memory, cognition, behavior, sensory, and motor functions are negatively impacted. Public health issues, such as noncommunicable diseases, which are a leading cause of death and morbidity among the elderly, are important concerns.[1,2] Protein degradation, different environmental factors, mitochondrial problems, familial history[3], aberrant protein buildup in neurons, etc. are some of the causes of neurodegenerative illnesses; nevertheless, aging is thought to be a key issue in neurodegenerative diseases.[4] Alzheimer's disease (AD), characterized by diffuse brain atrophy, Parkinson's disease, characterized by nigrostriatal neurons deprived of dopamine, Huntington's disease (H) characterized by spiny, medium-sized striatal neurons deprived of dopamine, and Parkinson's disease (PD) had been included in the classification of NDs previously. NDs were also used to describe other conditions such essential tremor or primary dystonia. There are many symptoms that NDs share, many of which overlap, as well as some clinical characteristics that are shared by all NDs, including a relentless progression that continues for years or even decades, and a wide range of symptoms that range from memory and cognitive deficits to mobility, speech, and breathing impairments.[5] The world of plants is the source of many contemporary synthetic medications, and it was not until about 200 years ago that herbal therapies gave rise to the primary pharmacopeias. Traditional medical practices experienced a sharp decline as clinical and basic pharmacology emerged as significant subfields.[6] However, research on herbal therapy is still ongoing for a range of conditions, including neurological and mental issues. There are multiple reasons why this issue exists. In the first place, patients are dissatisfied with traditional therapy; in the second place, they view herbal medicines as being in

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line with their personal values and beliefs; and in the third place, patients want autonomy over their medical decisions.[7] In addition to phytoconstituents, extracts may also have the ability to selectively bind to brain receptors, a factor that may make herbal medications an important part of the treatment of neurological disorders.[8,9] Many natural agents have been suggested for the treatment of neurodegenerative illnesses as supplements and/or supports to conventional pharmaceuticals.[10] Because these compounds exhibit a variety of neuroprotective properties, their usage in NDs has been extensively documented in numerous literatures.[11-14] The primary neuroprotective targets of natural products include oxidative stress, inflammation, protein misfolding, apoptosis, mitochondrial malfunction, and excitotoxicity.[14-18]

Its name comes from the Tamil word Veliparuthi, the Sanskrit word Attaravaruni, and the Hindi word Utranajutuka. A member of the family Asclepiadaceae, *Pergularia daemia* can be found in humid tropical zones.[19] This perennial herb grows untamed along Indian roadsides.[20] It has traditionally been used for anthelmintics, laxatives, expectorants, and antipyretics. It is also used to treat intermittent fevers associated with malaria and diarrhea in infants.[21-23] This plant's latex is used to treat sores and toothaches.[24] A treatment for fever and cold using stem bark. In its aerial parts, various pharmacological properties have been described, including hepatoprotective, antifertility, antidiabetic, analgesic, antipyretic, and anti-inflammatory effects.[25-27] Cardenolides, alkaloids, and saponins have all been studied phytochemically in relation to the plant. It was discovered that the plant contained a variety of steroidal chemicals including triterpenes.[28] *P. daemia* is examined based on this background study for its phytochemical properties and neuroprotective capabilities.

Overview of Neurodegenerative Diseases

The Molecular pathogenesis in neurodegenerative diseases were described in Figure 1.

Parkinson's Disease

The motor system of the brain is the primary affected area in Parkinson's disease (PD). Cells that produce dopamine are degenerate or die in this disease. A variety of factors contribute to the development of the condition, including oxidative stress, mitochondrial dysfunction, protein misfolding, excitotoxicity caused by a variety of biochemical pathways, lysosome dysfunction, chaperone-mediated autophagy, and Lewy bodies. There is a common accumulation of Lewy bodies, which contain neurofilament protein and ubiquitinatedsynuclein, in the olfactory region and lower areas of the brain stem. The disease further worsens, spreading to the middlebrain, forebrain, and neocortex, eventually affecting the entire brain. Alzheimer's disease, Parkinson's disease, and Huntington's disease are neurological conditions associated with aging that receive a lot of research attention today.[29,30]

Alzheimer's Disease

As senile plaques accumulate in the hippocampus region of the brain, Alzheimer's disease (AD) progresses and irreversibly weakens the brain's cognitive abilities.[31] As one ages, their capacity for self-healing gradually declines, making age a significant risk factor for neurodegenerative diseases. There are two types of Alzheimer's disease: random AD and familial/genetic AD. In cases of hereditary or familial AD, the illness manifests itself at a very young age; in contrast, sporadic AD typically affects older adults. A mutation in the amyloid precursor protein causes the disorder. Moreover, some of the pathological conditions of the disease include the production of plaque and neurofibrillary tangles containing phosphorylated tau and beta amyloid proteins. Amyloid precursor protein (APP) is a protein made up of an extracellular region and a transmembrane region. As one of the primary factors that are linked to sporadic AD, APP is cleaved by b and c secretases, resulting in the formation of 4 kDaAb peptides.[32]

Huntington's Disease

A genetic mutation in the chromosome 4 genes is thought to be the cause of Huntington's illness. Moment disorder is the hallmark of the illness, which often manifests in a person's fourth or fifth decade of life and continues to worsen for ten to twenty years afterward. Juveniles with the condition are rarely reported to have the more severe signs, such as stiffness. CAG repeats (cytosine, adenine, and guanine) are elongated in this autosomal disease, and thus determine the time when symptoms manifest. An N-terminal polyglutamic strand is formed upon the development of the mutant huntingtin protein caused by CAG repeats. Although each person experiences the symptoms differently, mental instability and behavioral abnormalities are among the most prevalent signs of Huntington's disease.[33]

P. daemia: Taxonomic Description

The perennial twining herb *P. daemia* is milky-sapient. Several meter-high stems are covered in hair, with delicate leaves on

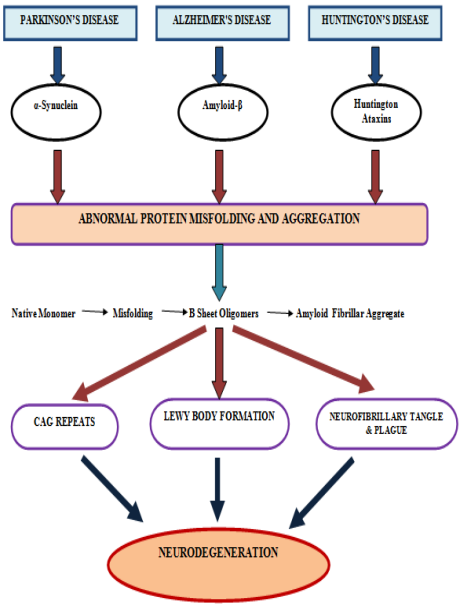

Figure 1: Molecular pathogenesis in neurodegenerative diseases

(A) Whole plant

(B) Flower

Figure 2: *P. daemia*

either side. Petioles are pubescent, 2 to 6.3 cm in length, and have ciliate, hairy borders. Its thin leaves have a diameter between 5 and 10 cm, and they are heart-shaped, broadly ovate, or glabrous. An axillary pseudo umbel and long peduncles support the flowers. The pendulous is open in the evenings. The tall, fringed lobes of corella are either creamy white or greenish white in color (Figure 2).

Habitat

Tropical and subtropical climates are the most common environments for *P. daemia* populations, especially in India, Africa, Arabia, Malaya, Pakistan, and Afghanistan. A hedge trim to 900 m often contains this species, while a hedge trim to 1000 m is more likely to contain it in the Himalayas. Ethnomedical uses of *P. daemia* were described in Figure 3.

Phytochemicals in *P. daemia*

It is essential to isolate and identify the bioactive molecules, as well as to extract, purify, and understand the purified compound's mode of action. As a result, current research efforts are concentrated on identifying bioactive components from medicinal plants as well as verifying previously reported therapeutic properties. Aromatic and medicinal plants' therapeutic and pharmacological potential is largely determined by the secondary metabolites they produce.[34] It has been reported that raw plant extracts can be used to treat a variety of diseases in some cases. Validation of bioactive phytochemicals requires both qualitative and quantitative methods of study. Qualitative analyses are performed on

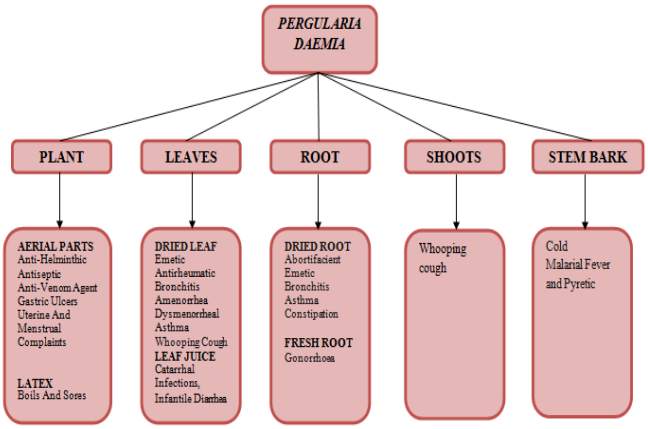

Figure 3: Ethno medicinal uses of *P. daemia*

phytochemicals. It contains alkaloids, terpenoids, steroids, tannins, glucosides, flavonoids, carbohydrates, acids, proteins, amino, oils, saponins, fixed gums, glycosides, and mucilage among others. Using phytochemicals to prepare the bioactive components to be extracted from plant sources is the first step. There is no difference between extracting phytocompounds from fresh or dried plants. When compared to dried powdered extraction, the freeze-drying extraction process often preserves higher amounts of phenolic content in plant samples.[24] Plant extracts are most prepared using solvent extractions, since they are simple to use, versatile, and efficient.

There is a variety of chemical compounds contained in *P. daemia*'s extract, including sitosterol, lupeol, lupeol acetate, amyrin, and an amino acid derivative. An entire dried plant is used to extract luteol-3-beta transcrotonate and oleanolic acid acetate. Betaine, hentriacontane, and pentacosanoicacid are also attributed to the plant, as well as magnesium and potassium carbonates, daemia extensive polypeptide, and calcium, magnesium, and potassium oxalate. Phytocompounds including calactin, calotropin, calotropigenin, dihydrocalotropigenin, protouscharin, uscharidin, and uscharin are present in seed extract. Coroglaucigenin, corotoxigenin, uscharidin, and uzarigenin extracts were also discovered in stems. Uscharidin, daemiaextensaglucoside, and the entire plant's inorganic salts, including Kcl and KNO3. Whereas young shoots and blossoms include flavonoids and saponins, dry stems contain hyperoside (flavonol).[34] An analysis of flavonoids extracted from *P. daemia* aerial sections identified them as the primary and significant phytochemicals. Several flavonoids, saponins, and hyperosides (flavonols) have been found in *P. daemia's* vegetative parts.[35] There are five types of phytocompounds: flavonoids, saponins, glycosides, phenols, phenolic and cyanogenic glycosides.[36] In plants, flavonoids include anthocyanins, coumarinlignans, catechins, and isocatechins. Flavonoids are antioxidant compounds that contribute to plant health.[37] Flavonoids and phenolic acids are two examples of polyphenolic chemicals that are abundant in fresh fruit juices and green leafy vegetables. These herbal medicines and antioxidant substances derived from herbs can

prevent diseases such as anti-inflammatory disorders, diabetes, cancer, stroke, atherosclerosis, and Alzheimer's disease. Numerous beneficial properties, including antibacterial, anti-inflammatory, and immunomodulatory action, are exhibited by flavonoids. Anthocyanidins, isoflavones, flavones, flavanols, and flavanones are the significant subclasses of flavonoids. Conversely, there are several medicinal plants that include large amounts of unidentified active ingredients. The flavonoids and other bioactive substances found in *P. daemia* were among these. There has been an increase in the popularity of natural therapies such as quercetin, kaempferol, myricetin, and morin as natural therapies are developed.[38,39]

The Effect of *P. Daemia* –on Neurodegenerative Diseases

Exploring *P. daemia's* antioxidant activity and neuroprotective benefits was the goal of this review. Moreover, oxidative stress can cause many serious health problems for humans. In response to a stressor, reactive oxygen species (ROS) and reactive nitrogen species (RNS) were released in excess. These reactive species contribute to the development of degenerative disorders. Electron transport releases dangerous radicals such as nitric oxide, reactive hydroxyl radicals, peroxyl radicals, and hydrogen peroxide.[40] An overabundance of reactive oxygen species (ROS/RNS) causes the defense mechanism to fail by releasing oxidant chemicals. Antioxidants are substances that serve as oxygen scavengers, chelate catalytic metals, and interfere with the oxidation process to neutralize free radicals. Free radicals cause oxidative damage, which decreases the risk of developing several diseases caused by free radicals. Our blood plasma contains an array of antioxidant molecules, including glutathione peroxidase, catalase, ascorbic acid, vitamin E, albumin, transferrin, ceruloplasmin, and tocopherol, quinines, ascorbic acid, and uric acid.By converting ROS/RNS into a stable molecule, antioxidants work to stop biological system damage.

There have been numerous reports of synthetic antioxidants being used by the pharmaceutical and food industries in the past few years, which are hazardous to human health. There are many examples of butylated hydroquinone, such as propyl gallate and butylatedhydroxyanisole. Conversely, a variety of highly antioxidant-active isolated chemicals from medicinal plants showed minimal or no adverse effects. It was determined that the antioxidant activity of *P. daemia* extracts could be measured by suppressing two synthetic free radicals, namely 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2,2′-azino-bis ((3-ethylbenzothiazoline-6-sulphonic acid) (ABTS). Like gallic acid, the methanolic preparation of a specific component of *P. daemia* was incredibly effective in reducing nitric oxide free radicals. This extract had a significantly higher ABTS IC50 value than gallic acid, which was 19.72 mg/mL. Similarly, the IC_{50} values for the DPPH scavenging activity of gallic acid and extract were 33.36 and 34.12 mg/mL, respectively. According to a study comparing *P. daemia* extract to gallic acid, it showed exceptional nitric oxide scavenging properties.[41] Despite this, a leaf extract from *P. daemia* dilute in 70% ethanol displayed marked antioxidative activity against DPPH free radicals comparable to ascorbic acid. The EC_{50} values of leaves range from 0.149 to 0.699 mg/mL; the EC_{50} values for flowers and leaves are similar. There was also an increase in antioxidant activity associated with lower EC_{50} values. In addition to alkaloids, phytosterols, flavonoids, tannins, phenols, triterpenes and saponins, plant extracts also contain phytochemicals. Possibly, this is why they are antioxidants.[42,43]

CONCLUSION

There are several similarities between these diseases on a molecular and cellular level, including inflammation, necroptosis, and apoptosis. Our hypothesis is that *P. daemia* demonstrated exceptional neuroprotective and antioxidative properties based on surveys of the literature and traditional reports. Antiapoptotic pathways could be involved in mediating this impact. Pharmacologically active substances and phytochemicals are present in medicinal plants. In *P. daemia* preparations, flavonoids and cardenolides are present, both of which have biological activity. Neurodegenerative diseases may benefit from phytochemicals' anti-inflammatory, antioxidant, and anticholinesterase properties in the future. The overall application of herbal medicine offers encouraging substitutes for existing neurodegeneration disorders.

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REFERENCES

1. David M. Wilson III, Mark R. Cookson, Ludo Van Den Bosch, Henrik Zetterberg, David M. Holtzman, Ilse Dewachter. *Hallmarks of neurodegenerative diseases***.**Cell 2023; 186: 693-714.DOI:https://doi.org/10.1016/j.cell.2022.12.032
2. GBD. 2015. Neurological Disorders Collaborator Group. Global, regional, and national burden of neurological disorders during 1990-2015: A systematic analysis for the global burden of disease study 2015. *Lancet Neurology*. 2017;16: 877–897.https://doi.org/10.1016/S1474-4422(17)30299-5
3. Beal MF. Mitochondria take center stage in aging and neurodegeneration. *Ann Neurology,*58(4); 2005: 495–505. https://doi.org/10.1002/ana.20624
4. Barnham KJ, Masters CL, Bush AI.Neurodegenerative diseases and oxidative stress.*Drug Discovery,*2004; 3:205–214. https://doi.org/10.1038/nrd1330
5. Hung CW, Chen YC, Hsieh WL, Chiou SH, Kao CL. Ageing and neurodegenerative diseases. *Ageing Research Review*, 2010; 9:S36–S46. https://doi.org/10.1016/j.arr.2010.08.006
6. JayaramRajangam, ArunPrasathLakshaman, Narhari N Patel, KarthikeyanElumalai, R.Prakash. DifferntialPharmacokinectic Interplay of Atrovastatin on Lacosamide and Levetiracetam on

Experimental convulsions in mice. Current drug metabolism.2023; Vol. 24(9).http://dx.doi.org/10.2174/1389200224092311192349097. S. Akhondzadeh, S.H. Abbasi, Herbal medicine in the treatment of Alzheimer's disease. *American Journal of Alzheimer's Disease & Other Dementias®.*2006; 21: 113–118. https://doi.org/10.1177/1533317506021002118. A. M, N A, Effects of medicinal plants on Alzheimer's disease and memory deficits, *Neural Regeneration. Research.*2017; 12: 660–670. DOI: https://doi.org/10.4103/1673-5374.2051089. 8. K. Lundstrom, H.T. Pham, L.D. Dinh, Interaction of plant extracts with central nervous system receptors, *Medicines*, 2017; 4. https://doi.org/10.3390/medicines40100129. PrakashRamakrishnanan, JayaramRajangamb, Binoy Varghese Cherianc, Jose PrakashDharmian. Croton hirtus attenuating streptozotocin-induced neuroinflammation in rats.Digital Chinese Medicine.Volume 6, Issue 3, September 2023, Pages 295-306.https://doi.org/10.1016/j.dcmed.2023.10.00511. Srivastava P, Yadav R.S. Efficacy of Natural Compounds in Neurodegenerative Disorders. In Glutamate and ATP at the Interface of Metabolism and Signaling in the Brain; Springer Science and Business Media LLC: Berlin, Germany, 2016; 12: 107–123.https://doi.org/10.1007/978-3-319-28383-8_712. Lökk J, Nilsson M. Frequency, type and factors associated with the use of complementary and alternative medicine in patients with Parkinson's disease at a neurological outpatient clinic. *Parkinsonism and Related Disorder.*2010; 16: 540–544.https://doi.org/10.1016/j.parkreldis.2010.06.00713. Prakash R, Ramanathan. Protective effect of non-selective COX inhibitor in Lipopolysaccharide induced neuroinflammation rats through NFκB pathway. Current Trends in Biotechnology and Pharmacy.Vol. 16 (1) 2022. http://dx.doi.org/10.5530/ctbp.2022.2s.3614. 13. Panda S.S, Jhanji N. Natural Products as Potential anti-Alzheimer Agents. *Current Medicinal Chemistry.* 2018.https://doi.org/10.2174/092986732666619061811361315. Leonoudakis D, Rane A, Angeli S, Lithgow G.J, Andersen J.K, Chinta, S.J. Anti-Inflammatory and Neuroprotective Role of Natural Product Securinine in Activated Glial Cells: Implications for Parkinson's Disease. *Mediators of Inflammation*. 2017; 2017: 8302636. https://doi.org/10.1155/2017/830263616. Bagli E, Goussia A, Moschos M.M, Agnantis N, Kitsos G. Natural Compounds and Neuroprotection: Mechanisms of Action and Novel Delivery Systems. *In Vivo,* 2016; 30: 535–547.https://doi.org/10.3390/ijms2020517017. Prakash R, Panneerselvam P, Dhivya R, Parthiban R, Subash V. Amelioration of Cognitive Deficits, Oxidative Damage, Neurochemical Alteration by Bauhinia purpurea (stem bark) on Scopolamine Induced Amnesia. Journal of Young Pharmacists. 2020; 12(3): 231-236.https://dx.doi.org/10.5530/jyp.2020.12.6618. Venkatesan R, Ji E, Kim, S.Y. Phytochemicals That Regulate Neurodegenerative Disease by Targeting Neurotrophins: A Comprehensive Review. *Biomed Research International*. 2015: 1–22. https://doi.org/10.1155/2015/81406819. Deshpande P, Gogia N, Singh A. Exploring the efficacy of natural products in alleviating Alzheimer's disease. *Neural Regeneration Research*.2019; 14: 1321–1329.https://doi.org/10.4103%2F1673-5374.25350920. Khare CP. Indian Medicinal Plants (An Illustrated Dictionary). New York: Springer Science and Business Media; 2007; 472.21. Yoganarasimhan SN. Medicinal plants of India. Bangalore: Interline Publishing Pvt. Ltd.; 2000; 1.22. Kirtikar KR, Basu BD. Indian Medicinal Plants, Vol.III. Dehardun: International Book Distributors; 1999; 1616 – 1617.23. NadkaraniAk. Indian MateriaMedica. Bombay; Popular PrakashanPvt Ltd; 1976; 1: 430.24. Anonymous. Indian Medicinal Plants (a compendium of 500 species). Hyderabad: Orient Longman Ltd; 1995; 4: 386 -389.25. Hebbar SS, Harsha VH, Shripathi V, Hegde GR. Ethnomedicine of Dharward district in Karnataka, Indiaplants used in oral health care. *JournalEthno pharmacology,* 2004; 94: 261-266.https://doi.org/10.1016/j.jep.2004.04.02126. Prakash R, Sandhya E, Ramya N, Dhivya R, Priyadarshini M, SakthiPriya B. Neuroprotective activity of Ethanolic extract of *TinosporaCordifolia* on Lipopolysaccharide induced Neuroinflammation. Translational Biomedicine, Vol.8, 4:135. DOI: 10.21767/2172-0479.10013527. GolamSadik, Gafur MA, Shah AlamBhuiyan M, KhurshidAlam AHM, Helal U Biswas M, Parvez Hassan, Abdul Mannan, Omar Faruk Khan M, Chowdhury AKA. Antifertility activity of *P. daemia*.*The Sciences* 2001a; 1(1): 22-24.DOI: 10.3923/jms.2001.22.2428. Wahi AK, Ravi J, Hemalatha S, Singh PN. Anti diabetic activity of *Daemiaextensa. Journal of Natural Remedy,* 2002; 2(1): 80-83. https://doi.org/10.18311/jnr/2002/35029. Prakash R, Chandrasekar T and Muralidharan P. Cognitive enhancing, anti acetylcholinesterase and antioxidant properties of *TagetesPatula* on scopalamine induced amnesia in mice. International Journal of Green Pharmacy, Vol. 9, (3), july-sep2015.https://doi.org/10.22377/ijgp.v9i3.45530. Eftekharzadeh B, Hyman BT, Wegmann S. Structural studies on the mechanism of protein aggregation in agerelated neurodegenerative diseases. *Mechanism of Ageing and Development,* 2016; 156:1–13. https://doi.org/10.1016/j.mad.2016.03.00131. Hung CW, Chen YC, Hsieh WL, Chiou SH, Kao CL. Ageing and neurodegenerative diseases. *Ageing Research Review.* 2010; 9S:S36–S46. https://doi.org/10.1016/j.arr.2010.08.00632. Alzheimer's Association: 2010 Alzheimer's disease facts and figures. *Alzheimers Dementia* 6:158-194.https://doi.org/10.1016/j.jalz.2010.01.00933. Hebert SS, Horre K, Nicolai L, Papadopoulou AS, Mandemakers W, Silahtaroglu AN, Kauppinen S, Delacourte A, Strooper BD. Loss of microRNA cluster miR-29a/b-1 in sporadic Alzheimer's disease correlates with increased BACE1/ b-secretase expression. *Proceedings of the National Academic Sciences,* 2008; 105(17):6415–642034. Li SH, Li XJ. Huntingtin–protein interactions and the pathogenesis of Huntington's disease. Trends Genet, 2004; 20(3):146–154. https://doi.org/10.1038/sj.embor.740025035. Ananth DA, Rameshkumar A, Jeyadevi R, Aseervatham GSB, Sripriya J, Bose PC*, et al.*Amelioratory effect of flavonoids rich *Pergularia daemia* extract against CFA induced arthritic rats. *Biomedicine and Pharmacotherapy.*2016; 80:244–52.https://doi.org/10.1016/j.biopha.2016.03.01936. Subramanian SS, Nair A. Flavonoids of some asclepiadaceous plants. *Phytochemistry.* 1968;7(9): 1703–4.https://doi.org/10.1016/S0031-9422(00)88630-637. Shahidi F, McDonald J, Chandrasekara A, Zhong Y. Phytochemicals of foods, beverages and fruit vinegars: chemistry and health effects. *Asian Pacific Journal of Clinical Nutrition*.

2008;17(S1):380–2.DOI: 10.12691/ajfn-5-4-1
38. Aqil F, Ahmad I, Mehmood Z. Antioxidant and free radical scavenging properties of twelve traditionally used Indian medicinal plants. *Turkish Journal Bioliogy*. 2006;30(3):177–83.
39. López-Lázaro M. Distribution and biological activities of the flavonoid luteolin. *MiniReviews in Medicinal Chemistry*. 2009;9(1): 31–59. http://dx.doi.org/10.2174/138955709787001712
40. Lin J-K, Weng M-S. Flavonoids as nutraceuticals. In: The science of flavonoids: Springer; 2006; 213–38.
41. Emerit J, Edeas M, Bricaire F. Neurodegenerative diseases and oxidative stress. *Biomedicine Pharmacotherapy*. 2004;58(1): 39–46.https://doi.org/10.1016/j.biopha.2003.11.004
42. Cook NC, Samman S. Flavonoids—chemistry, metabolism, cardioprotective effects, and dietary sources. *Journal of Nutritional Biochemistry*. 1996;7(2):66–76. https://doi.org/10.1016/S0955-2863(95)00168-9
43. Karthishwaran K, Mirunalini S. Assessment of the antioxidant potential of *Pergularia daemia* (Forsk.) extract in vitro and in vivo experiments on hamster buccal pouch carcinogenesis. *Asian Pacific Journal of Tropical Disease*. 2012;2:S509–S16. https://doi.org/10.1016/S2222-1808(12)60212-6
44. Sarkodie J, Squire S, Kretchy I, Domozoro C, Ahiagbe K, Twumasi M. The antihyperglycemic, antioxidant, and antimicrobial activities of Ehretiacymosa.*Journal of Pharmacognosy and Phytochemistry*.2015;4(3):105–11.https://doi.org/10.3390/molecules2821740