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**Keywords:** Alzheimer's disease, Amyloid- $\beta$ , Antioxidant, *Coriandrum sativum, Curcuma longa*, Medicinal plant, Phytochemical, *Withania somnifera*.

#### Abstract:

Alzheimer's disease (AD) is caused due to degeneration of the brain cells that leads to dementia, which is characterized by impaired thinking, remembering and independence in personal daily activities. It is a multifactorial neurodegenerative disorder caused primarily due to the accumulation of amyloid- $\beta$  (A $\beta$ ) and tau protein hyperphosphorylation, which induce oxidative stress that affects a wide range of the cerebral cortex and hippocampus. Furthermore, various risk factors like increasing ageing, head injuries, infections, and environmental factors also contribute to the occurrence of the disease. Globally more than 57.4 million people are affected with AD and the cases are increasing day by day. Still, only two classes of drugs i.e. cholinesterase inhibitors and N-methyl d-aspartate (NMDA) antagonists, are available to treat symptoms of AD, however there is no cure or prevention of the disease. Phytochemicals isolated from medicinal plants are proven to be effective in various diseases. Here, we aimed to discuss the effects of three native medicinal plants (Curcuma longa, Withania somnifera & Coriandrum sativum) in AD. A potent phytochemical curcumin found in Curcuma longa has antiinflammatory and antioxidant properties, reducing oxidative stress and preventing the formation of amyloid- $\beta$  plaque. Bioactive components such as Witanopherin, witanolides A-Y etc. of Withania somnifera are found to be effective in decreasing the level of inflammatory mediators like IL-1 $\beta$ , Il-6, TNF- $\alpha$ , MCP-1. Moreover, these phytochemicals inhibit amyloidß and tau protein accumulation, thereby preventing AD. Coriandrum sativum contains active phenolic components which have antioxidant property. Volatile oil from C. sativum proven to be effective for the prevention and reversal of the conditions of AD. Therefore, using these indigenous medicinal plants for the treatment of patients with Alzheimer's disease is a better alternative as these natural products are very effective with no side effects.

#### **Introduction:**

Extremely frequent entities of neurogenetic disorders and Alzheimer's disease (AD) clearly demonstrate the range of neurological diseases that lead to unfathomable problems among people and their families worldwide. These terms refer to neurogenetic disorders as they cover

**Shubham Ghosh** PGT Biology, HolyMother's Academy, Fulwar, Dhanbad, Jharkhand, India **Biplab Bhowmik** Department of Zoology, Diamond Harbour Women's University, Sarisha, West Bengal, India E-mail: Panchakotbb@gmail.com Saptarshi Chatterjee Department Universitv of Burdwan, Bardhaman, Bengal, India Zoology, West of Susmita Mondal\* Department of Zoology, Diamond Harbour Women's University, Sarisha, West Bengal, India E-mail: 🙆 susmita.dhwu@gmail.com; Orcid iD: 🔟 https://orcid.org/ 0009-0003-8119-2197 \*Corresponding Author: susmita.dhwu@gmail.com

© International Academic Publishing House, 2023 Mrs. Bhanumati Sarkar, Dr. (Professor) Surjyo Jyoti Biswas, Dr. Alok Chandra Samal & Dr. Akhil Pandey (eds.), The Basic Handbook of Indian Ethnobotany and Traditional Medicine [Volume: 2]. ISBN: 978-81-962683-5-0; pp. 46-55; Published online: 15th December, 2023 a spectrum of disorders due to genetic mutations that alleviate the nervous system's structure and function. These pathologies commonly come with extremely diverse symptoms like cognitive impairments, motor dysfunctions and sensory dysfunctions, which present complicated diagnostic and management choices for healthcare providers (Dey & Guha, 2020; Haloi et al., 2023).

Alzheimer's disease (AD), being a neurodegenerative disorder, affects the aged people most. The name of the disease comes after Alois Alzheimer, a German neuropathologist who discovered it in 1906. The disease appears with memory loss, impaired performance, and deterioration in thinking ability as its main symptoms. Externally, AD resembles severe depression. Patient affected with AD exhibit emotional impairment like irritability, frustration and hostility (Ballard et al., 2011; Alzheimer's disease facts and figures, 2010). Due to amyloid-beta peptide's (A $\beta$ ) accumulation in the brain, neuritic plaques and neurofibrillary tangles are formed, resulting in Alzheimer's disease (De-Paula et al., 2012). AD is one of the most common modes of dementia and it contributes around 75% of all dementia reports. The effect of the disease is most prevalent in people above 65 years whether. Around 2-5% of cases are found at early ages. According to the latest reports, around 57.4 million people will be affected by it, which evokes global concern (Ray et al., 2023). Only some treatments are there to improve the quality of life of AD victims, but no cure is available right now (Yiannopoulou & Papageorgiou, 2020; Livingston et al., 2020). Herbal medicines contribute to the prevention of the progress of the disease and now-a-days, these are very much trending using medicinal plants for the production of drugs (Abascal & Yarnell, 2004; Perry et al., 1999). Medicinal plants (nervines) have the properties to improve the function of the nervous system and memory (Manyam, 1999; Mishra et al., 2000). According to phytochemical studies, various plant compounds effectively reduce inflammation. They exhibit anti-amyloidogenic, antioxidant, anti-cholinesterase and hypolipidemic effects (Howes et al., 2003; Kennedy & Wightman, 2011; Kumar, 2006; Manyam, 1999).

# Neuropathy of Alzheimer's disease:

The neuropathology of AD exhibit two types of lesions:

- i. Positive lesions- In this case, neurofibrillary tangles, dystrophic neurites and amyloid plaques are found in the brain. All of these are due to accumulation.
- Negative lessons- These are exhibited by atrophy caused by synaptic, neural and neuropil loss. In addition, injury of cholinergic neurons, neuroinflammation and oxidative stress also results in neurodegeneration (Serrano-Pozo, 2011; Spires-Jones, 2014; Singh, 2016).

# Molecular mechanism of AD:

A $\beta$  pathology and neurofibrillary tau pathology are the two main characteristics of Alzheimer's. A lot of studies have been conducted on the A $\beta$  pathology (Pimplikar, 2009). As a therapeutic target to manage the disease, tau came to light after the failure of A $\beta$  based clinical

trials. A lot of analysis reveals that, though Tau pathologies are exhibited in various neurodegenerative issues, the proteins are structurally different in each case (Avila et al., 2004). Cell-to-cell transmission of tau and conversion of normal tau to abnormal forms may be important points in administering AD treatment (Hasegawa, 2016). An unusual deposition of  $\beta$ -amyloid protein in the brain is shown in the cases of AD. In the fibrillar form of the protein, it has a neurotoxic effect as it provokes free radical formation and interrupts glucose transportation to neurons. Due to the accumulation of senile plaques, microglial cells produce toxins that destroy diseased and healthy neurons, enhancing the brain's inflammatory response (Tiwari et al., 2019).



Figure 1. Pathophysiology of Alzheimer's disease

# **Effects of Plant products on AD:**

In this review, three very popular indigenous medicinal plants (*Curcuma longa, Withania somnifera & Coriandrum sativum*) will be discussed from the perspective of therapeutics against AD.

# Curcuma longa:

*Curcuma longa*, commonly known as Turmeric, is very well known in Ayurveda (Indian system of Medicine) for its anti-inflammatory activity. It also exhibits anti-cancer properties (Shishodia, 2005; Ammon & Wahl, 1991). *Curcuma longa* belongs to the family Zingiberaceae, the ginger family. It is used as a spice in India. Main active compounds of turmeric are curcumin, curcuminoids and turmerone oil (Agarwal et al., 2007). The epidemiological study found that AD cases are 4.4-fold lower in Southeast Asia because of using turmeric in their daily life as a spice (Ganguli et al., 2000). The anti-inflammatory

property of *Curcuma longa* is also responsible for controlling AD (Breitner et al., 1995). Curcumin decreases plaque deposition when they are given turmeric for feeding (Begum et al., 2008). It also checks the oxidative damage and reverses the A $\beta$  pathology (Lim et al., 2001). Curcumin prevents plaque development, including the reduction of plaque levels, if injected into the brains of the mice. The strong antioxidant and anti-inflammatory properties of curcumin decrease the symptoms of Alzheimer's (Yang et al., 2005). In vitro, curcumin is more potent than Vitamin E in preventing lipid peroxidation and neutralizing the reactive oxygen species (Butterfield et al., 2002). No acute toxicity was observed after receiving 2000, 10,000 or 50,000 ppm of turmeric oleoresin to groups of male and female rats and mice for 13 weeks and 2 years in a Technical Report Series, National Toxicology Program CAS NO. 8024-37-1.

A randomized, placebo-controlled, double-blind clinical trial of curcumin in 27 patients having Alzheimer consuming 4g per day was found safe (Baum et al., 2008). If administered orally, more clinical trials are required to determine curcumin's efficacy (Belkacemi et al., 2011).



Figure 2. Schematic representation of the effects of bioactive components from *Curcuma longa* in Alzheimer's disease

### Withania somnifera:

In Ayurveda, the uses of *Withania somnifera* (Ashwagandha) are extensive. It belongs to Solanaceae family. It is a nervine tonic that helps relieve stress (adaptogens), prevent free

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radicals and boost immunity (Mishra et al., 2000; Russo et al., 2001; Bhattacharjee, 2020). It is reported in a monograph of Alternative Medicine Review in 2004 that, Ashwagandha is different from the other adaptogens, it exhibits a calming effect rather stimulating, so it may be helpful for peoples with AD. Witanolides and alkaloids are two main active substances present in this plant. Witanopherin A, witanolides A-Y, witanone, witadomniferin A, and witasomniferols are the witanolides and witanin, somniferin, somnin, tropin, somniferinin, pseudowitanin, pseudotropin, choline, kuskohigrin, isopeletierin, and anaferin are the alkaloids (John, 2014). The study revealed that ashwagandha is potent to neutralize the  $\beta$ - amyloid, the leading cause of AD (Kurapati et al., 2013). A study exhibited inhibition of amyloid β-42, and decreased the level of IL-1  $\beta$ , Il-6, TNF- $\alpha$ , MCP-1 and lipid peroxidation after oral administration of vitanon (a compound isolated from ashwagandha) in rat. Vitanon also reduced the activity of  $\beta$  and  $\gamma$ -secretase (the main cause of the formation of neurotoxic aggregates of  $\beta$ -amyloid (Pandey et al., 2018). Withaferin A, a witanolides of this plant, inhibits tau protein accumulation and  $\beta$ -amyloid aggregation and, thus, has a promising effect to prevent AD. The compound also regulates the heat shock proteins (HSPs), which express more with cell exposure towards stress (Das et al., 2021).



Figure 3. Schematic representation of the effects of bioactive components from *Withania* somnifera in Alzheimer's disease (Abbreviations: NF-κβ: nuclear factor kappa B IL-1β: interleukin-1β; IL-8: interleukin-8; TNFa: tumor necrosis factor-α, STAT: signal transducers and activators of transcription; Nrf 2: nuclear factor erythroid 2–related factor; ROS: reactive oxygen species)

## Coriandrum sativum:

*Coriandrum sativum* is an herb originating in Mediterranean areas (Yeung and Bowra,2011). It is generally used to treat digestive problems, diarrhea, colic, and other gastrointestinal medicine in Iranian traditional medicine (Zargari, 1991). Due to having phenolic compounds the plant shows hepatoprotective properties (Pandey et al., 2011). *C. sativum* also exhibit antioxidant activity in different organs (Kansal et al., 2011). Studies show that leaves of plants have the potential to improve memory and prevent aging in mice dose-dependently (Mani et al., 2011). The plant's hydroalcoholic extract (50,100 &200 mg/kg) prevents pentylenetetrazole-induced neuronal damage (Pourzaki et al., 2017). The efficacy of an active ingredient, volatile oil from *C. sativum*, after daily inhalation (1-3%) for 21 days was evaluated, which exhibited an improved deleterious effect of AD and reversed the condition of AD. It is reported that animals treated with volatile oil have a very low chance of amyloid deposition, In addition the oil from *C. sativum* also contributes to the improvement of hippocampal tissues, reduction of sodium dis-mutase, and MDA depending upon dose (Cioanca et al., 2013).

# **Conclusion:**

Alzheimer's disease is a problem of global concern. The number of victims is increasing vigorously. Aged people (>65 years) are more prone to this disease, but the disease can be started at a very early age. No drastic changes will occur, so can't be marked at early levels always. No cure has been invented against this culprit till today. The treatments available in the market prevent further development and maintenance of quality of life. Medicinal plants may be a lantern to the darkness in this difficult situation (Sarkar et al., 2016, 2021, 2022). As various study depicts the efficiency of various plant products against AD is hopeful, more studies should be done in this area. The studies show that plant products are comparatively safe and effective. With the advancement of science, plant products may be a breakthrough treatment procedure against Alzheimer's disease.

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