



Review Article

A PROMISING APPROACH FOR THE TREATMENT BY DEMENTIA DISEASE WITH THE HELP OF HERBAL DRUGS

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ABSTRACT

Dementia is the end of cognitive functioning thinking, remembering, and reasoning. It can lead to feelings of helplessness and a change in personality. As dementia progresses, it becomes more difficult for a person to do basic activities of daily living, such as feed oneself, without the help of others. By 2050, it is anticipated that this number would increase to 131 million due to an ageing population worldwide. The mildest stages of dementia occur when a person's ability to function begins to be affected. Alzheimer's disease, vascular dementia, lewy body dementia, and front temporal dementia are the four most common types of dementia. In dementia, medicinal plants show effects on antioxidant, acetylcholinesterase (AChE), glutathione levels, NMDA receptors, and secretase. The herbal plants have been utilized to treat age-related cognitive decline, and today herbal therapy is well-known worldwide. This review article discusses many medicinal plants that may be used to treat dementia.

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INTRODUCTION:

Dementia is a malady that can be caused by a variety of diseases that damage nerve cells over time and catastrophe the brain, usually resulting in impaired cognitive function (i.e., the ability to process thoughts) decrease a normal biological consequence of aging. Consciousness is unaffected, but deterioration of cognitive function is often conveyed and occasionally led by variations in mood, emotional regulation, behavior, or encouragement. Dementia affects people practically, mentally, culturally, and financially, as well as their caretakers, family members, and society at large¹. Dementia is frequently misunderstood, which leads to stigmatization and obstacles to treatment and detection. In fact, it is no longer dementia but a major neurocognitive disorder (MND)². The syndrome is frequently brought on by a collection of chronic, neurodegenerative brain conditions that manifest in old age. At both the household and social levels, dementia care is extremely expensive. Thus, it poses a significant challenge in terms of both global economy and public health³. The human brain has uncommon cognitive capacities. This is often due in specific to the extended neo cortex and its abnormal helplessness to plastic changes. This permitted for the advancement of such human capacities as awareness,

recognition, memory, discourse, and theoretical considering⁴. The hallmarks of Alzheimer's disease, which is the model for degenerative dementias, are the buildup of beta-amyloid protein farther of the neurons and the buildup of protein (referred to as tau tangles) inside the neurons. Cerebrovascular shocks that result in pathological alterations to the brain that affect cognition are a component of vascular dementias⁵. The gradual loss of cognitive functions can be caused by brain disorders such as Alzheimer's disease (AD) or other factors such as toxicity, infection, circulatory system and lung abnormalities, resulting in decreased oxygen supply to the brain, nutrition those results in deficiency, vitamin deficiency Vitamin B12 deficiency, tumors and others⁶. The primary one is the cellular level deterioration in energy metabolism brought on by ageing. It causes the homeostasis, which is essential for brain function, to be disturbed and leads to metabolic abnormalities that gradually worsen. These lead to a number of age-related behavioural dysfunctions, including reduced mental and physical activity and sleep issues. These dysfunctions worsen the pathophysiological alterations in the brain, which cause a significant loss of nerve cells⁷. Dementia results from the ageing organism's self-destructive process, which is expanding quickly. It is the

suppression of environmental contact, which is the purpose of life.

DEMENTIA vs. ALZHEIMER'S DISEASE

The term dementia refers to a condition that is characterized by a steady decline in cognitive abilities. Apathy, agitation, and sadness are among the neuropsychiatric symptoms. The patient increasingly becomes reliant on other people to carry out everyday tasks as the illness worsens⁸. The fundamental reason for the dementia disorder is one of a few hidden sicknesses or conditions. Every one of these problems or illnesses is recognized by a specific arrangement of signs and side effects as well as possible neurosciences⁹. A majority of dementia cases are caused by Alzheimer's disease. Secondly, vascular dementia is one of the most prevalent causes¹⁰. The signs of dementia include misplacing things, impaired judgments, having difficulty while understanding the language, personality changes¹¹. Differentiating between dementia subtypes might be challenging. Yet, the majority of dementias are inoperable, inevitable, and developing. The condition is impacted by

various gamble factors, including propelling age, genetic factors, head injuries, vascular issues, diseases, and ecological elements¹². Both physical and metabolic abnormalities in the brain can cause dementia. Agitation, irritability, moodiness, anxiety, apathy, delusion, depressive symptoms, disinhibition, euphoria, hallucinations, lack of appetite, and sleep difficulties are some of the behavioral and psychological signs of dementia¹³. The signs of mild Alzheimer's disease include forgetting dates or being aware of one's actual location, asking the same questions repeatedly or inattentive what you've just learnt. The warning indicators of a severe case of Alzheimer's include loss of weight without eating much, lack of bladder and bowel control, having trouble in swallowing, seizures. Aspiration pneumonia is a leading cause of mortality for those with Alzheimer's. At the point when an individual can't swallow as expected, food or fluids enter the lungs rather than air, prompting the improvement of this sort of pneumonia¹⁴.

PATHOPHYSIOLOGY OF DEMENTIA

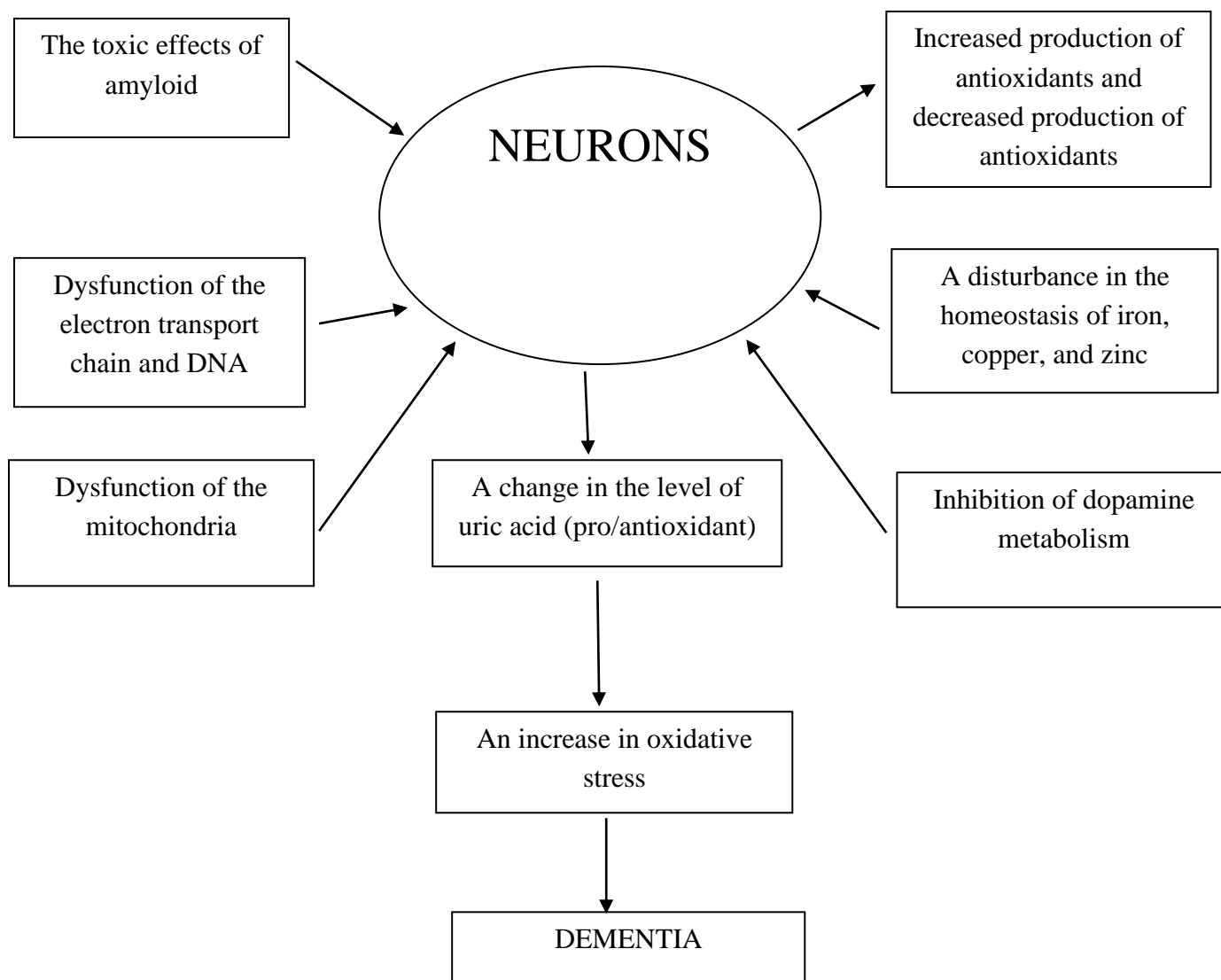


Fig. 1. Representation of pathophysiology of dementia¹⁵

ETIOLOGY OF DEMENTIA:

A person's age is the primary risk factor for the majority of dementias, with the prevalence almost twice every five years beyond the age of 65. Early onset is quite rare and frequently points to a hereditary basis in the case of AD. A large portion of these occasions are brought about by single quality changes at one of three loci (β amyloid precursor protein, presenilin1

and presenilin2) Environmental and genetic variables are both involved in late-onset AD¹⁶. High risk categories for dementia include elderly people with a family background of dementia in first-degree family members (especially of the beginning stage kind) and hereditary helplessness. Also, persons who have had head traumas and persistent depression in the past are known to be at a higher risk,

so they should be on the lookout for memory issues in later life¹⁷. Having high cardiovascular risk scores which include hypertension, diabetes, hypercholesterolemia, and smoking raises one's chances of developing dementia, whether the exposure is assessed in middle age or a few years before dementia first manifests¹⁸. Although diabetes is a known risk factor, more new research has linked metabolic syndrome to acute cognitive impairment and insulin resistance to worse executive ability. For India and other developing nations, the hazards associated with metabolic syndrome, diabetes, hypertension, and smoking are particularly relevant¹⁹.

PREVELANCE OF DEMENTIA IN INDIA:

India's population in 2023 is estimated to be around 1.423 billion in which 58% of the total population²⁰. As the population ages, dementia becomes an issue, and India is predicted to have one of the highest numbers of elderly people with dementia. This shows that dementia is already a major problem in India and is projected to get worse over the next 20 to 30 years. It is anticipated that the percentage of dementia sufferers in the 60 to 75 age range would rise consistently over time. On the other side, beyond 2030, a sharp rise in dementia is anticipated in

the over 75 age group²¹. Just one in ten dementia sufferers in India receives a diagnosis, treatment, or care, leaving a treatment or service gap estimated to be close to 90%. The causes of this are several, but the primary ones seem to be low levels of public and professional knowledge of dementia, a lack of trained or specialized human resource capacity for the care of persons with dementia, and a lack of public health priority for dementia. The existing paradigm of specialized dementia healthcare provision is neither likely to be cost-effective nor likely to offer comprehensive protection to satisfy the rising service demand. There is a need to include community healthcare providers trained to carry out particular duties in dementia care provision. There is a lack of spreading awareness, and a lack of sufficient specialist trained resources in low- and middle-income countries like India. According to evidence, primary care physicians may offer dementia care with outcomes that are comparable to those of specialized care. In fact, doctors who specialize in basic care have effectively handled memory clinics. Nonetheless, research is still needed in the field of post-diagnosis ongoing treatment for dementia in primary care²².

DIFFERENT TYPES OF DEMENTIA WITH ITS CAUSES

Traditionally, there are two forms of dementia: irreversible dementia and reversible dementia. Certain varieties of dementia are accompanied with permanent brain damage i.e., irreversible dementia. Alzheimer's disease is the prototype of irreversible dementia. Various dementia can be reparable i.e., reversible dementia²³. Medications (any anticholinergic drug),

emotional-depression, metabolic (hypothyroid), infection (syphilis, AIDS), anemia (vitamin B12 or folate deficiency), The many permanent and reversible dementia causes are depicted. It is critical to recognize that people may have risk factors and clinical signs of more than one kind of dementia²⁴. The table given below describes the types of dementia and causes behind the dementia disease.

Table 1: The causes and types of dementia²⁵

SL. NO.	TYPES OF DEMENTIA	CAUSE OF DEMENTIA
1.	Irreversible dementia	<ul style="list-style-type: none"> • Alzheimer's disease • Frontotemporal dementia • Vascular dementia • Dementia with Lewy bodies • Parkinson's dementia
2.	Reversible dementias (Neurosurgical conditions)	<ul style="list-style-type: none"> • Subdural hematoma • Normal pressure hydrocephalus • Intracranial tumors • Intracranial empyema or abscess
3.	Infections	<ul style="list-style-type: none"> • Meningitis (tubercular, fungal, malignant) • HIV dementia • Neurosyphilis • Lyme's disease • Whipple's disease
4.	Inflammatory/autoimmune cause	<ul style="list-style-type: none"> • Sarcoidosis • Multiple sclerosis • Systemic lupus erythematosus • Sjogren's syndrome • Autoimmune limbic encephalitis
5.	Metabolic conditions	<ul style="list-style-type: none"> • Hashimotos encephalitis • Hypo- and hyper- parathyroidism • Pituitary insufficiency • Hypercalcemia • Cushing's disease

		<ul style="list-style-type: none"> • Addison’s disease • Hypoglycemia • Wilson’s disease
6.	Organ Failure	<ul style="list-style-type: none"> • Chronic liver failure • Hepatic encephalopathy • Chronic respiratory failure • Pulmonary insufficiency • Chronic renal failure
7.	Nutritional deficiencies	<ul style="list-style-type: none"> • Vitamin deficiencies (A, B1, B6, B12, and folate) • Iron deficiency
8.	Substance use Alcohol abuse	<ul style="list-style-type: none"> • Toxins/toxicity with metals Arsenic • Mercury • Aluminum • Lithium • Lead • Manganese
9.	Trauma	Head injury - any injury that effect the scalp, brain, or skull area.

IMPORTANCE OF HERBAL DRUGS:

Natural compounds produced from plants called "herbal medicines" are used to cure ailments in traditional local or regional medicine. These substances are intricate blends of organic compounds that can originate from any unprocessed or refined portion of a plant. Every civilization on earth has used herbal medicine at some point²⁶. Various traditional medical practices have different philosophical and methodological approaches, which are affected by social, environmental, and geographic variables, but they all prioritize a holistic approach to health. Well-known

herbal medical systems, including Traditional Chinese Medicine and Ayurveda, adhere to the fundamental principle that the focus of treatment should be on health rather than illness²⁷. Individuals can improve their general health and concentrate on their general wellbeing rather than a specific illness by employing therapeutic herbs. There are many reasons for this, including out of balance minds, bodies, and environments. Herbal medicine first appeared in ancient societies²⁸. Plant materials are used to treat illnesses in herbal medicine, sometimes called herbalism or botanical medicine.

Several diverse societies throughout the world have employed herbal medicine since the dawn of humanity. Several remedies, including those for malaria, warts, intestinal issues, heart diseases, and chronic pain, are developed by pharmacists and physicians who study about folk medicine²⁹. In spite of the fact that there are more than 500,000 different medicinal plant species in the world, most of them haven't yet been explored for their medical properties, the future is bright for these plants. The characteristics of herbal plants are divided into two parts i.e., synergic and preventive medicine. Synergic medication: Plants' constituent parts communicate simultaneously, considering the potential for their applications to commend, mischief, or even balance the impacts of different purposes. Plant-based ingredients have shown to be particularly effective in treating difficult instances like cancer disorders³⁰. Preventative medicine: It has been established that some plant components are notable for their capacity to delay the onset of certain illnesses. This will lessen the adverse effects of synthetic therapy by reducing the usage of chemical therapies that are utilized when the disease is already established³¹.

THE EMPHASIS OF HERBAL DRUGS IN THE TREATMENT OF DEMENSIA AND ITS RELATED CAUSES:

The treatment of dementia disease and memory loss involves the use of medicinal herbs in a substantial way. Ayurvedic, homoeopathic, unani, and sidha systems of medicine are among the most significant traditional therapeutic modalities. Because the Unani system of medicine typically gives a highly scientific kind of healthcare as a heavenly gift, the medical community is increasingly interested in medicinal plants³². Fundamentally, the traditional medical system is preventative, protecting, nourishing, and curative. Traditional medicines treat patients safely and effectively while having little to no negative effects. It includes using therapeutic herbs to treat dementia and improves overall health and wellbeing. Indeed, a lot of pharmaceutical medications are made from synthetic variations of naturally occurring substances found in plants³³. The use of plants as medication to cure illness and improve health, frequently without having any noticeable adverse effects, has drawn more scientific attention in recent years as interest in herbal therapy has grown. The nervous system in the human body controls and directs the body's many

voluntary and involuntary functions³⁴. Because of the relationship between the central nervous system and the autonomic nervous system, several medicines that impact the CNS can also have effects on the autonomic nervous system. A serious issue with global health is memory loss. It is advised to use a variety of medicinal herbs to improve memory. Due to their perceived affordability, safety, and

efficacy, herbal medications are growing in popularity. In fact, the use of herbal remedies for diseases connected to memory has only lately received backing from scientific investigations³⁵. The table 2 given below are some of the drugs that have been proven positive for the treatment of dementia.

TABLE2: INDIAN HERBAL MEDICINE FOR THE TREATMENT OF DEMENTIA

SL. NO	NAME OF THE HERB	BIOLOGICAL SOURCE	MECHANISM OF ACTION
1.	Ashwagandha ³⁶	<i>Withania somnifera</i> , fam. Solanaceae ³⁶	Ashwagandha contains L-dopa in a natural composition. Memory is improved by using cholinergic channels. Improves learning abilities and psychological stability. Anxiolytic impact of GABA-mimetic action ³⁷ . Inhibiting Cholinesterase and so maintaining Acetylcholine for a longer period of time. Slowing of tolerance to morphine's analgesic effects ³⁸ . Axon and dendrite outgrowth is stimulated, resulting in neuritis regeneration and synaptic repair ³⁹ .
2.	Turmeric ⁴⁰	It is obtained from the rhizome of <i>Curcuma longa</i> , belongs to	Curcuminoids have been displayed to have high antioxidant, as proven by the concealment of free radical creation and movement. It lessens low-thickness lipoprotein oxidation and free

		the family of Zingiberaceae ⁴⁰ .	extremists, which prompt neuro-degeneration in Alzheimer's sickness as well as in other neurodegenerative ailments like Huntington's and Parkinson's illness ⁴¹ . It also boosted the activity of sodium-potassium ATPase, which generally decreases with age. Curcumin has also been found in another research to protect cells against beta A (1-42) damage via an antioxidant mechanism ⁴² . Curcumin protects brain mitochondria from many forms of oxidative damage. Curcumin pretreatment protects brain mitochondria against peroxynitrite ⁴³ .
3.	Brahmi ⁴⁴	(<i>Bacopa monneri</i>) It is belong to the family of Plantaginaceae (Plantain family) ⁴⁴	Brahmi therapy was discovered to increase the expression of numerous antioxidant molecules such as SOD and GSH. Additionally, Brahmi investigated ways to mitigate H ₂ O ₂ -mediated oxidative damage ⁴⁵ . Lipoxygenase enzyme degrades the cell membrane by deoxygenating polyunsaturated fatty acids, resulting in cell degeneration ⁴⁶ .
4.	Shankhpushpi ⁴⁷	(<i>Convolvulus pluricaulis</i>) is a common plant in India. It belongs to the family Convolvulaceae ⁴⁷	It has been suggested that Shankhpushpi has a calming impact through controlling the body's hormone synthetic substances, adrenaline and cortisol ⁴⁸ . There is a considerable expansion in the quantity of dendritic convergences, branch focuses, and dendritic cycles beginning from the cell collections of neurons ⁴⁹ .
5.	Jyotishmati ⁵⁰	<i>Celastrus paniculatus</i> Wild (<i>Celastraceae</i>) is a key therapeutic plant in Ayurvedic	Aqueous concentration of CP seeds show cell reinforcement and cognizance upgrading impacts. Because of their antioxidant characteristics and capacity to stimulate antioxidant enzymes, CP extracts rescued neuronal cells from H ₂ O ₂ -induced damage.

		medicine. It belongs to the family Celastraceae ⁵⁰	Through altering glutamate receptor activity, CP extracts also rescued neuronal cells from glutamate-induced damage ⁵¹ . Furthermore, it protected neuronal cells through their free radical scavenging activities, capacity to reduce lipid peroxidation, and ability to stimulate the antioxidant enzyme catalase. Seed have dose-dependent cholinergic action, which improves memory performance ⁵² .
6.	Jatamansi ⁵³	(<i>Nardostachys jatamansi</i>) It belong to the family of Valerianaceae ⁵³	<i>N. jatamansi</i> exhibited strong antioxidant activity and dramatically corrected stress-induced increases in LPO and NO levels as well as a reduction in catalase activity in the brain. <i>N. jatamansi</i> has substantial anti-stress potential, which might be attributed to its antioxidant activity ⁵⁴ . Glutathione-transferase, glutathione reductase, and catalase activity, catecholamine quantitation, and dopaminergic D2 receptor binding affects the expression of tyrosine hydroxylase. <i>N. jatamansi</i> substantially and dose-dependently recovered the increase in drug-induced rotations and reduction in locomotor activity and muscle coordination caused by 6-OHDA injections ⁵⁵ .
7.	Clitoria ternatea ⁵⁶	<i>C. ternatea</i> belongs to family Fabaceae commonly called “butterfly” ⁵⁶	The effects of dopamine, noradrenaline, serotonin, and acetylcholine on behaviour were seen on experimental models. The <i>C. ternatea</i> extract reduced the time required to occupy the centre platform or transfer latency in the raised plus maze and enhanced the discriminating index in the object recognition test, demonstrating nootropic action ⁵⁷ .

8.	Desmodium gangeticum ⁵⁸	<i>Desmodium gangeticum</i> (<i>D. gangeticum</i>), belonging to the family Fabaceae ⁵⁸	Cholinergic deficiency occurs in the brains of Alzheimer's disease and vascular dementia patients ⁵⁹ . Anticholinesterase activity has been observed for indol-3-alkyl-amines and b-carbolines isolated from <i>D. gangeticum</i> . Phenytoin is well-known for lowering hippocampus ACh concentrations and causing cognitive impairment ⁶⁰ .
9.	Eclipta Species ⁶¹	<i>Eclipta Alba</i> belonging to the Asteraceae family ⁶¹ .	EA mitigated scopolamine-induced learning and memory impairments while also lowering scopolamine-induced increases in AChE activity and oxidative stress levels in the brain. It is possible to infer that <i>Eclipta alba</i> has a considerable protective effect against scopolamine-induced memory losses in mice, which can be linked to its anti-AChE and anti-oxidant properties ⁶² .
10.	Moringa oleifera ⁶³	<i>Moringa oleifera</i> (<i>M. oleifera</i>) belonging to the family Moringaceae ⁶³	<i>M. oleifera</i> leaves extract's effect on spatial memory as well as neurodegeneration, oxidative stress indicators, and the change of AChE activity in the hippocampus ⁶⁴ . The study showed that the lowered oxidative stress and better cholinergic function may contribute to the <i>M. oleifera</i> leaf extract's ability to improve memory. It in turn boosted local blood flow and suppressed monoamine oxidase (MAO), resulting in the improved dopaminergic activity ⁶⁵ .

CONCLUSION:

Probably the most important characteristic that sets humans apart from other animals is memory. Unfortunately, memory problems can occur for a variety of causes, and when they do, a person cannot reach their full potential. Drugs and herbal treatments have coexisted for millennia that used to improve people's memory. Compared to other types of medication, herbal remedies are proven to be more effective in treating specific ailments. If not combined with other chemicals, they are reputed to be entirely natural. Reverse pharmacological methods provide effective development frameworks for herbal medicines. Regarding food and treatment alternatives, the Ayurveda medical system has recently gained more and more popularity. Early Ayurveda herbal supplement development relied solely on epidemiologic data, without any knowledge of the route of action. To lay out "verification of idea" and a "method of activity," a seriously demanding logical technique with further developed quality has been utilized. To give new practical prompts Promotion and other age-related neurodegenerative sicknesses, it is trusted that the vigorous Ayurvedic information base will be joined with combinatorial sciences and high-throughput screening methods to make it more straightforward to involve ayurvedic items and definitions

in drug revelation missions and advancement processes.

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