Review Article

POTENTIAL OF NATURAL SUBSTANCE USAGE IN SOUTHEAST ASIA FOR MEMORY ENHANCEMENT: A REVIEW

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Abstract

The use of natural substance-based supplements and treatments for mental wellness is increasingly gaining attention. Southeast Asia, with its rich heritage of medicinal practices and cultural reliance on natural remedies, presents a unique opportunity to explore such interventions. Delightex is actively collaborating with research partners in Southeast Asia to investigate natural substances that may enhance mental well-being and create enriching experiences. Memory, defined as the capacity to record, retain and recall sensory stimuli, events and information, is a fundamental aspect of mental health. Memory loss and Alzheimer's Disease (AD) are significant and growing concerns worldwide, particularly due to aging populations. Nootropics are generally well tolerated and typically mild. However, occasional complications can still occur. Hence, it is important to explore more natural alternatives for memory enhancement or treatment of memory loss. In this review, following an initial comprehensive literature search on mental well-being, we focused on memory improvement, identified and summarized 57 natural substances from 32 families with potential memory-enhancing effects. This review highlights their traditional use in Southeast Asia and examines the scientific evidence supporting their efficacy in enhancing memory and potential as nootropics alternatives. ***ASEAN Journal of Psychiatry, Vol. 25 (8) September, 2024; 1-18.***

Keywords: Memory Enhancement; Memory Improvement; Memory Booster; Alzheimer's Disease (AD); Nootropics; Natural Substance; Southeast Asia

Introduction

Memory encompasses the storage of information, the mental representation of experiences and the mental processes involved in learning, storing and retrieving information [1]. Human memory can be categorized into three essential types: Sensory memory, short-term memory and long-term memory [2]. Information processing begins in sensory memory, where it is held for a brief moment. It then transitions to short-term memory, which serves as the subject's working memory and may eventually be consolidated into long-term memory [2].

Memory loss, a central and highly feared consequence of aging, is also the signal symptom of dementia [3]. Memory issues, such as poor recall, low retention, difficulty concentrating and weak analytical skills and are prevalent in today's world [4]. In some cases, these issues may escalate into more serious conditions, such as Alzheimer's Disease (AD) or schizophrenia [4,5]. Memory loss is often one of the initial symptoms of AD reported by patients with and their caretakers [6]. As of 2019, the global prevalence of AD was estimated at 57.4 million cases and this number could rise to 152.8 million by 2050 [7]. The increasing prevalence of AD, coupled with its strong impact on individuals and families, highlights the critical need for effective treatments and preventive strategies for AD and memory loss.

Nootropics, commonly referred to as smart drugs, encompass a diverse class of pharmacological agents that enhance cognitive

functions, including thinking, learning and memory, particularly in conditions where these capabilities are impaired [8]. Nootropics work by enhancing the brain's glucose and oxygen supply, exhibiting antihypoxic properties and protecting brain tissue from neurotoxicity [8-10]. Classical Nootropic Compounds include Deanol Dimethylaminoethanol (DMAE), Meclofenoxate, Nicergoline, Piracetam and Pyritinol [8].

Additionally, some substances exhibit simultaneous nootropic, hemorheological and vasodilatory effects. Examples of these include vinpocetine, naftidrofuryl and dihydroergotoxine [8]. While there are benefits of nootropic drugs and nootropics are generally well tolerated and typically mild, there are still concerns over side effects, addictiveness and potential abuse of drugs [11,12]. Meanwhile, options to explore natural substances based on the traditional use have been regained interest as an alternative to those modern medicines. For example, traditional systems such as Ayurveda, have identified several herbs and plants with memory benefits [13,14]. Several species of plants have been selected for testing as nootropic agents because of their use in traditional medicine. Notable examples include *Gingko biloba*, *Panax ginseng*, *Paullinia cupana* and *Rhodiola rosea* [8].

Southeast Asia, with its rich biodiversity and traditional medicinal practices, offers a plethora of natural substances that could potentially enhance memory. However, there is a lack of comprehensive literature reviews summarizing the use of natural substances for memory enhancement in Southeast Asian regions. This review explores natural substances from this region, summarizing their taxonomic classification, the parts used, traditional applications and the scientific evidence supporting their potential for memory enhancement and their role as alternatives to nootropics. The bioactive compounds of highlighted substances are also discussed.

Methodology

Through collaborations with Southeast Asian research partners, Delightex is exploring natural substances that may enhance mental well-being, in this review, we have refereed to works done by Delightex's research partners from Philippines (the University of Santo Tomas, the University of Antique) and Delightex's Vietnam research team. The criteria of natural substance search using key words such as 'natural substances,' 'Southeast Asian countries' and 'medicinal plants' using databases and other online sources. Based on the broad search on mental wellness, we further narrowed specific natural substances with potential memory-enhancing effects, utilizing terms such as 'memory enhancement', 'memory boosting', 'memory impairment', 'memory loss' and 'nootropics'. This review discusses selected plants traditionally used or supported by scientific evidence for memory enhancement in Southeast Asian countries.

Results and Discussion

Following comprehensive reviews of mental well-being enhancing natural substances conducted across Southeast Asia by Delightex's research partners, including the University of Santo Tomas, the University of Antique and Delightex's research team in Vietnam, we further focused on identifying natural substances with memory-enhancing properties. This investigation led to the identification of 57 natural substances (Table 1). The table provides detailed information for each substance, including its botanical family, scientific name, utilized part, traditional applications (if available) and supporting scientific evidence for its memory improvement effects.

In this review, the substances have been categorized and analyzed by botanical family to offer a more comprehensive understanding of their potential roles in promoting mental well-being. Figure 1 depicts the distribution of memory enhancing natural substances in Southeast Asia by families. 57 memory enhancing natural substances are from 32 families. Among them, 14% natural substances are from the Lamiaceae family, the Fabaceae family and followed by the Malvaceae family (5.3%).

Plant families

The Lamiaceae family, also known as the mint or deadnettle family, comprises dicotyledonous flowering plants distributed globally. The enlarged Lamiaceae contains about 236 genera and about 6900 to 7200 species [15]. The Lamiaceae family is known for its high essential oil content and is also rich in polyphenolic compounds and terpenoids [16]. This review has listed 8 substances within this family (Table 1).

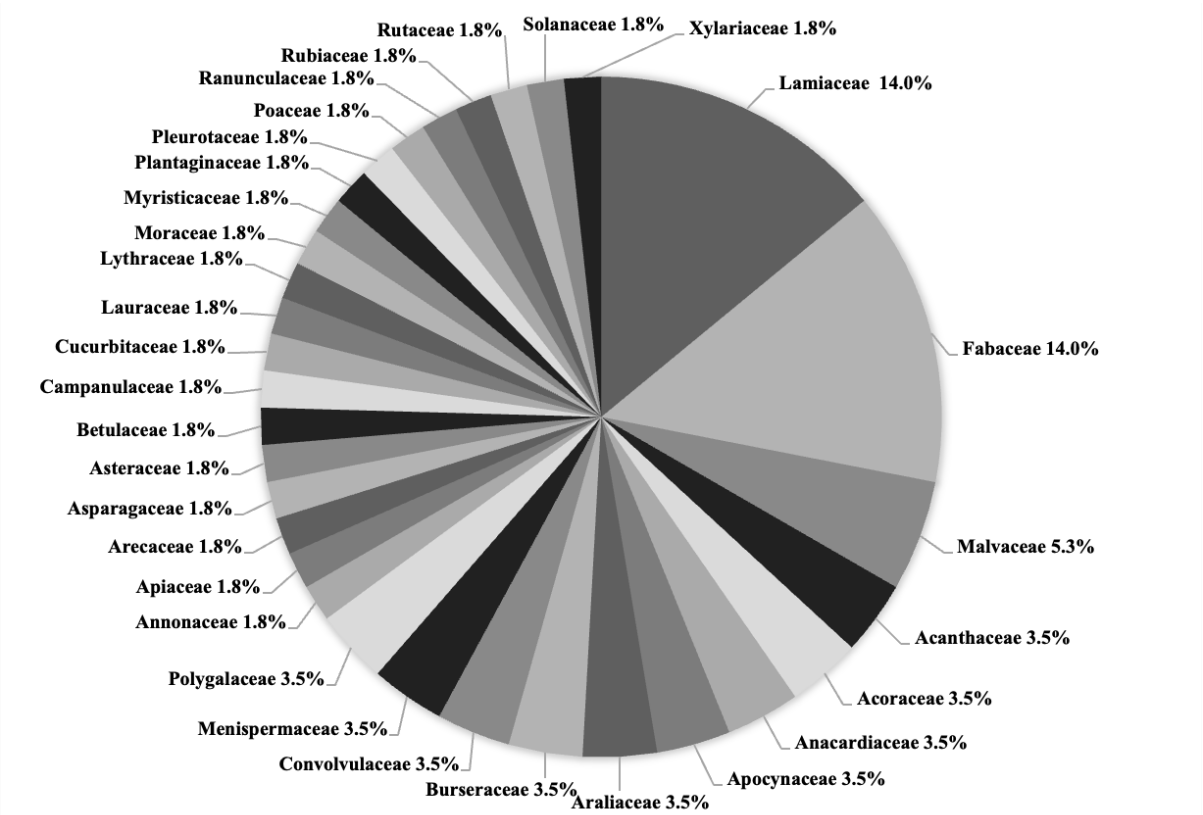

Figure 1. Pie chart categorizing memory-enhancing natural substances from Southeast Asia by family names.

Hyptis suaveolens, commonly known as pokok kemangi in Malaysia, amotan, suobkabayo, or loko-loko in the Philippines and kara or maeng lak kha in Thailand [17]. It is found in southeast Asian countries such as Cambodia, Thailand, Indonesia, Malaysia, Vietnam and Philippines [18]. *H. suaveolens* is a rich source of medicinally significant phytochemicals, including essential oils, tannins, saponins, phenols, flavonoids, terpenoids, alkaloids and sterols. Main components identified in *H. suaveolens* essential oil include 1,8-Cineole (Eucalyptol), Sabinene, β-Caryophyllene and β-elemene [19]. These compounds belong to the terpene classes of monoterpene hydrocarbons and sesquiterpene hydrocarbons [19]. Traditionally, plant extracts of *H. suaveolens* were used as a memory aid [20]. In India, it was referred to as Chan or Wilaiti Tulsi, and the morning soup, made by mixing it with corn known as bate was believed to aid memory [21].

Salvia rosmarinus, commonly known as rosemary, is an evergreen, bushy shrub that thrives along the Mediterranean coast and in sub-Himalayan regions [22]. It is called dumero, romero and rosmiro in Philippines [23]. In Philippines, a leaf infusion of rosemary is utilized as eyewash for mild catarrhal conjunctivitis, as vapor baths for the treatment of rheumatism, paralysis and early-stage catarrhs and for bathing postpartum women [23]. The main bioactive compounds in rosemary are triterpenes, phenolic diterpenes and phenolic acids including rosmarinic acid, carnosic acid, rosmanol, carnosol, ursolic acid and betulinic acid [24,25]. In traditional medicine, rosemary is believed to fortify the brain and refresh the memory [23]. The rosemary extracts have clinical effects on mood, learning, memory, pain, anxiety and sleep. Rosemary (500 mg administered twice daily for one month) has been shown to enhance both prospective and retrospective memory in a study involving 68 university students [26]. Additionally, Rosemary powder (750 mg), a dose comparable to typical culinary use, has demonstrated positive effects on memory speed and the efficiency of retrieving information from both episodic and working memory in 28 older adults (mean age: 75 years) [27]. Their finding suggests that rosemary may be a valuable memory enhancer.

Vitex negundo, commonly known as Chinese

chaste tree, is native to tropical Eastern and Southern Africa and Asia [28]. In Southeast Asia, it is found in to countries such as Bhutan, Cambodia, Indonesia, Malaysia, Myanmar, Philippines, Thailand and Vietnam [28]. Kanwal et al. reported that treatment with *V. negundo* aqueous extracts (300 mg/kg) for 5 days reduced scopolamine-induced amnesia in rats by enhancing memory and learning through antioxidant effects and decreasing AChE activity [29]. The administration of hydroalcoholic extract of *V. negundo* leaves at doses of 250 mg/kg and 500 mg/kg over 8 days significantly enhanced learning and memory in mice [30]. This improvement may be attributed to AchE inhibition, antioxidant activity and/or enhanced cholinergic transmission and the nootropic activity could be associated with the presence of compounds such as flavonoids, triterpenoids, phenolic acids and lignans in the extract [30].

Family Fabaceae: The Fabaceae family, commonly known as the legume, bean, or pea family, is the third largest family in the plant kingdom, comprising approximately 19,500 species, which constitute about 7% of all flowering plants [31]. This review has listed and summarized 8 substances within this family (Table 1).

Arachis hypogaea, peanut is one of the most consumed oil seeds worldwide. Peanuts have spread to other parts of the world from South America [32]. Peanuts are extensively utilized in the culinary traditions of Southeast Asia, particularly in countries such as Malaysia, Vietnam and Indonesia, where they are commonly processed into spicy sauces. In the Philippines, peanut is a key ingredient in the traditional dish kare-kare and fried shelled peanuts are widely consumed as an affordable snack throughout the Philippines. Regular peanut and peanut butter consumption may improve memory function and stress response in healthy young adults. These effects appear to be linked to the intake of peanut polyphenols [33]. In this 6-month randomized controlled trial, participants consuming 25 g/day of skin-roasted peanuts or consuming 32 g/day of peanut butter have shown improved immediate memory after the intervention [33].

Clitoria ternatea, known as butterfly pea and blue pea in various countries is originated from tropical Asia countries. It is widely available in the Asian regions [34,35]. As a traditional Ayurveda medicine used as a brain tonic, memory and nootropic herb, butterfly pea flower plays an important role in nervine medicine as well as improving brain system and boosting memory [35]. Chronic oral administration of butterfly pea root extract for 28 days at doses of 200 mg/kg and 300 mg/kg effectively restored memory impairments in rats induced by Chronic Cerebral Hypoperfusion (CCH) [36].

Pueraria candollei var. mirifica is endemic to Thailand and is widely distributed in the country's deciduous forests, particularly at altitudes of 300 to 800 meters. It is called kwao khrua khaw (various spellings) in the Thai language [37]. It is most commonly and abundantly found in the northern, western and northeastern regions of Thailand [38,39]. The main bioactive phytochemicals of *P. mirifica* are phytoestrogens including isoflavonoids, coumestans and chromenes [40]. Traditionally, pounding the roots of *P. mirifica* and mixing them with cow's milk is believed to enhance memory [41]. *P. mirifica* extracts have demonstrated beneficial effects on cognitive deficits associated with menopause or estrogen depletion, primarily through its phytoestrogenic and antioxidant properties [42]. In the same study, it was found that the extracts at a daily dose of 25 mg/kg exerted anti-dementia effects that were almost equivalent to the effects elicited by 17β-estradiol at 1 μg/kg [42].

Family Malvaceae: The Malvaceae, commonly known as the mallow family, is a group of dicotyledonous flowering plants comprising approximately 244 genera and around 4,225 species. These species are distributed across regions ranging from tropical to temperate climates [43]. This review has explored 3 substances within this family (Table 1).

Abelmoschus manihot is cultivated particularly in the eastern parts of Indonesia and in Papua New Guinea [44]. In North Sulawesi, Indonesia, this plant is known as "gedi" and its leaves are a key ingredient in preparing porridge, a distinctive gourmet dish in North Sulawesi cuisine [45]. More than 128 phytochemical compounds have been extracted and identified from the flowers, seeds, stems and leaves of *A. manihot* [46]. These compounds primarily include flavonoids, amino acids, nucleosides, polysaccharides, organic acids, steroids and volatile oils [46]. The hydroalcoholic extract of *A. manihot* flowers has been shown to alleviate learning and memory impairments caused by sleep deprivation in mice [47]. This effect may be attributed to its antioxidant capacity

and enhanced BDNF/TrkB/GluR1 levels in the hippocampal memory [47].

Thespesia populnea commonly known as Indian tulip tree. The species is native to Australia, China and India but can also be found on rocky coasts such as in Malaysia and other countries in SEA including Cambodia, Indonesia, Philippines and Thailand [48]. *T. populnea* contains glycosides such as quercetin, gossypol, β-sitosterol and sesquiterpene, lupenone and lupeol [49,50]. Thespesenone and dehydrooxoperezinone-6-methyl ether have been isolated from the red hardwood, while alanine, arginine, methionine and tryptophan have been identified in the seeds [51,52]. The bark of *T. populnea* shows potential as a memory-enhancing agent. Oral administration of ethanol bark extract of *T. populnea* at doses of 200 mg/kg and 400 mg/kg for 7 days significantly improved memory in both young and aged mice [53].

Other families: *Areca catechu*, belongs to the Arecaceae family, a species of palm native to the Philippines, is primarily grown for its areca nuts [54,55]. It is known by various common names, including betelnut palm, arecanut, betel palm, betel-nut, supari palm, pinang palm [56]. It is extensively cultivated in several Southeast Asian countries, including Malaysia, Indonesia, Cambodia, Laos, Myanmar, Thailand and Vietnam [57]. *A. catechu* contains alkaloids, polyphenols, polysaccharides, triterpenes, steroids, fatty acids and other components [58]. These compounds demonstrate a variety of bioactive functions, such as antibacterial, deworming, antiviral, antioxidant, anti-inflammatory and anti-tumour effects [58]. Extracts of arecanut have been reported to improve memory. Oral administration of methanol extracts of arecanut at a dose of 500 mg/kg for 21 days significantly improved memory and learning in rats [59]. Arecoline, the major alkaloid of arecanut, has been reported to enhance memory in both laboratory animals and humans, as summarized by Bhat et al [60]. For example, in humans, a 4 mg injection of arecoline significantly enhanced serial learning and reversed impaired learning behaviour induced by scopolamine, a cholinergic antagonist [61]. Additionally, a 4 mg dose of arecoline significantly improved picture recognition in Alzheimer's patients [62].

Bacopa monnieri also known as waterhyssop, thyme-leafed gratiola, bacopa and brahmi, is a perennial, creeping herb from the Plantaginaceae family. Bacopa is a medicinal herb native to South and Southeast Asia [63]. Ayurvedic medicine classifies Bacopa as a 'medhya rasayana' which refers to a category of herbs thought to enhance mental health, boost memory and intellect and support rejuvenation and longevity [64,65]. Preliminary clinical studies have suggested that Bacopa has the potential in ameliorating cognitive disorders, as well as prophylactic reduction of oxidative damage, neurotransmitter modulation and cognitive enhancement in healthy individuals [66]. Additionally, across six human randomized controlled trials were all conducted over 12 weeks have reported that 300 mg to 450 mg bacopa extract per day have improved performance on 9 of 17 tests in the domain of memory free recall [67]. *B. monnieri* is rich in a variety of distinct bioactive phytoconstituents, each offering a range of benefits. Among them, Bacopaside XI, bacopaside I and bacopasaponsin C, administered at a concentration of 50 mg/kg, demonstrated nootropic effects and reduced memory impairment in mice [68,69].

Table 1. List of natural substances in Southeast Asia countries and their usage for memory enhancement.

Family	*Scientific name*	Part	Scientific evidence and traditional knowledge (if available) on memory enhancement	References
Acanthaceae	*Peristrophe bicalyculata*	Leaf	The methanolic leaf extract improves memory performance in a rat model of type 2 diabetes mellitus	[70]
	Rhinacanthus nasutus	Leaf, root	The ethanol extracts from the leaves and roots have demonstrated a dose-dependent ability to reduce neuron cell death induced by both glutamate and amyloid-β exposure	[71]

Acoraceae	*Acorus calamus*	Root, Rhizome	In Ayurvedic medicine, rhizomes are used for treatment of epilepsy, schizophrenia and memory disorders The memory impairment in groups that received aqueous fraction at 600 mg/kg dose, was less than control Alpha-asarone, as a major component of the *A. calamus* ameliorates memory deficit in mice	[72-74]
	Acorus gramineus	Rhizome	Across 34 studies involving 1,431 animals, extracts or active components were found to significantly enhance learning and memory function	[75]
Anacardiaceae	*Rhus verniciflua*	Bark	Active component fesetin reduced memory deficits induced by scopolamine through activation of the CREB–BDNF pathway	[76]
	Spondias mombin	Leaf	Oral administration of aqueous extracts at 400mg/kg for 28 days improved learning and memory capabilities in rats	[77]
Annonaceae	*Annona squamosa*	Leaf	The leaf extract and its isolated constituent-anonaine demonstrated memory boosting and memory regaining effects in rats	[78]
Apiaceae	*Centella asiatica*	N/A	An Ayurvedic herb used to enhance memory and nerve function Water extracts (200 mg/kg/day, 2 weeks) attenuated amyloid-β-associated behavioral abnormalities in the Tg2576 mouse, a murine model of AD	[79]
Apocynaceae	*Catharanthus roseus*	Leaf, stem and root	Aqueous extract of leaf, stem and root have been shown to effectively inhibit AchE *in-vitro* and active compound serpentine displayed a strong activity against (AchE) *in-vitro*, suggesting a potential as a therapeutic agent for AD	[80]
	Tabernaemontana divaricata	Root	The ethanolic root extract acts as a reversible (AChE-I) and may offer potential as a novel therapeutic agent for AD	[81]

Araliaceae	*Eleutherococcus senticosus*	Leaf	Oral administration of the water extract for 17 days significantly enhanced object recognition memory; Pure compounds ciwujianoside C3, eleutheroside M, ciwujianoside B were administered orally for 17 days to normal mice and significantly enhanced object recognition memory	[82]
	Panax ginseng	Root	Oral administration of fermented cultured wild ginseng root extract (HLJG0701-β) (250 mg/kg, 8 weeks) resulted in memory improvement in mice	[83]
Arecaceae	*Areca catechu*	Fruit, seed, nut	Refer to the text above	
Asparagaceae	*Asparagus racemosus Willd*	Root	Administration of extract (200 mg/kg, 7 days) has shown a promising memory-enhancing effect in both young and aged mice	[84]
Asteraceae	*Achillea biebersteinii*	Aerial Part (stem, leaf and flower)	Inhalation of essential oil (1%, 3%) for 21 days significantly increased spontaneous alternation percentage, and decreased the working memory errors and reference memory errors in rats	[85]
Betulaceae	*Betula platyphylla*	Bark	Oral treatment using bark (BPB-316) significantly attenuated amyloid-β-induced memory impairment in mice	[86]
Burseraceae	*Commiphora caudata*	Leaf	Ethanolic leaves extract (200 mg/kg, 400 mg/kg, 27 days) enhanced learning and memory activity: Transfer Latency (TL), Time Taken To Reach Reward Chamber (TRC) and Swim Latency (SL) in comparison to scopolamine treated rats	[87]
	Garuga pinnata	Bark	Contains bioactive phytoconstituents, including alkaloids, tannins, phenols, and flavonoids, which possess free radical scavenging properties and memory-enhancing capabilities	[88]
Campanulaceae	*Platycodon grandiflorus*	Root	Administration of root to mice resulted in increased spontaneous alternation in the Y-maze test and promoted synaptogenesis in the hippocampus	[89]
Convolvulaceae	*Convolvulus pluricaulis*	Whole plant	Administration of extract (200 mg/kg, 7 days) has shown a promising memory-enhancing effect in both young and aged mice	[84]
	Ipomoea batatas	Tuber	Anthocyanins extracted from purple sweet potato demonstrate memory-enhancing effects, potentially linked to their antioxidant properties	[90]

Cucurbitaceae	*Cucurbita maxima*	Seed	Ethanolic seed extract (50 mg/kg, 100 mg/kg and 200 mg/kg) exhibited anxiolytic and antidepressant effects with memory improvement in mice	[91]
Fabaceae	*Mimosa pudica*	Leaf	Behavioral effects on learning and memory were augmented by leaf ethyl acetate extracts (200 mg/kg and 400 mg/kg)	[92]
	Albizia adianthifolia	Leaf	Aqueous extract (150 mg/kg, 300 mg/kg) plays an important role in spatial memory formation, especially on working and reference memories	[93]
	Arachis hypogaea	Seed, leaf	Refer to the text above	
	Cassia obtusifolia/ Senna obtusifolia	Seed	Ethanolic seed extract (50 mg/kg) attenuates memory impairment induced by scopolamine or 2VO and that these effects are mediated by enhancing the cholinergic nervous system *via* acetylcholinesterase inhibition	[94]
	Clitoria ternatea	Root, whole plant	Refer to the text above	
	Glycyrrhiza glabra	Root	Aqueous extracts (150 mg/kg) significantly improved learning and memory of mice	[95]
	Piliostigma thonningii	Stem, Bark	Aqueous and methanolic stem bark extract showed remarkable cognitive-enhancing activities which were reflected in significantly shorter transfer latencies, navigation distances, longer time spent in platform quadrant, and lower MDA levels compared to the negative control mice	[96]
	Pueraria candollei var. mirifica	Roots, tuber	Refer to the text above	

Lamiaceae	*Hyptis suaveolens*	Whole plant (except root)	Refer to the text above	
	Melissa officinalis	Leaf	Administration of ethanolic extract (200 mg/kg) could significantly enhance learning and memory in memory-impaired rats	[97]
	Prunella vulgaris var. lilacina	Flower	Ethanolic flower extract (25 mg/kg) significantly shortened escape latencies in training-trials. Furthermore, swimming times within the target zone during the probe-trial were significantly increased as compared with scopolamine-treated mice	[98]
	Salvia rosmarinus	Leaf	Refer to the text above	
	Salvia miltiorrhiza	Root	Subchronic administration of root extract (200 mg/kg) led to an improvement of long-term memory of rats	[99]
	Salvia officinalis	Leaf	*S. officinalis* aroma group performed significantly better than the control group on the quality of memory and secondary memory primary outcome factors from the test battery	[100]
	Scutellaria baicalensis	Root	Extracts (30 mg/kg) improved spatial memory functions and rescued neuronal cells immune-reactive to ChAT and the NMDA receptor subunit, NR2A, in the hippocampus of memory deficient rat model	[101]
	Vitex negundo	Leaf	Refer to the text above	
Lauraceae	*Cinnamomum zeylanicum*	Bark	Aqueous bark extract-treated animals exhibited an improved discrimination between a familiar object and a novel object, indicating the reversal of extract induced memory impairment. Extract also restored alteration in AChE activity and oxidative stress parameters in both brain parts	[102]
Lythraceae	*Lawsonia inermis*	Leaf	Extract at doses of 200 mg/kg and 400 mg/kg significant increased the inflexion ratio in elevated plus maze and increase in percentage alternation in Y-maze model compared to negative control animals	[103]

Malvaceae	*Abelmoschus manihot*	Flower	Refer to the text above	
	Abelmoschus moschatus	Seed	Oral administration of ethanolic seed extract (100 mg/kg, 200 mg/kg) for seven days demonstrated a dose-dependent improvement in memory in young mice and effectively reversed diazepam-induced memory deficits	[104]
	Thespesia populnea	Bark	Refer to the text above	
Menispermaceae	*Cissampelos pariera*	Root	The dose of 400mg/kg of ethanolic extract significantly improved learning and memory of mice	[105]
	Tiliacora triandra	Leaf	Leaf extract at doses of 300 mg/kg and 600 mg/kg significantly enhances spatial learning and learning flexibility. Only the 300 mg/kg dose showed a significant improvement in spatial memory	[106]
Moraceae	*Ficus racemosa*	Bark	Administration of the extract at two levels, 250 mg/kg and 500 mg/kg extract resulted in significant reduction in transfer latency on elevated plus-maze, which was used as an exteroceptive behavioural model to evaluate memory in rats	[107]
Myristicaceae	*Myristica fragrans*	Seed	Extract at the lowest dose of 5 mg/kg P.O. administered for 3 successive days significantly improved learning and memory of young and aged mice	[108]
Plantaginaceae	*Bacopa monnieri*	Whole plant/leaf	Refer to the text above	
Poaceae	*Cymbopogon citratusx*	Leaf	After the inhalation, the lemongrass essential oil enhanced their cognitive performance for the domains of the continuity of attention and the quality of memory, whereas the mood in terms of alertness and calmness was also increased	[109]
Pleurotaceae	*Pleurotus eryngii*	Fruiting Body	The ethanol extract of *P. ryngii* exhibits estrogen-like effects, providing potential benefits for alleviating depression and improving memory impairment in rats Feeding with *P. eryngii* for six weeks has promoted memory and learning capacity in an AD mouse model	[110, 111]

Polygalaceae	*Polygala japonica*	Root	A traditional medicine for treatment of variety of ailments, including anti-inflammatory, antibacterial, sedative and nootropic agent; Compound saponins can improve the learning and memory in mice	[112]
	Polygala tenuifolia	Root	The impaired spatial memory of the aged mice was partly reversed by extract (100 mg/kg and 200 mg/kg) as compared with the aged control mice. In stepdown tests, the nonspatial memory of the aged mice was improved by extract (100 mg/kg and 200 mg/kg)	[113]
Ranunculaceae	*Nigella sativa*	Seed	Hydro-alcoholic extract improved the LPS-induced learning and memory impairments in rats	[114]
Rutaceae	*Lunasia amara*	Bark	A traditional Ayurveda medicine as a brain tonic, memory and intelligence enhancer	N/A
Solanaceae	*Withania somnifera*	Root	Known as Ashwagandha, it has been traditionally used in Ayurvedic medicine as a substance to strengthen the nervous system; Root extract alleviated hypobaric hypoxia -induced memory impairment and neurodegeneration in the hippocampus by modulating corticosterone levels through nitric oxide pathways	[115,116]
Xylariaceae	*Xylaria nigripes*	Mycelium	Water extracts (300 mg/kg/day, 6 weeks) improved Rapid Eye Movement Sleep Deprivation (REMSD)-induced memory impairment in rats	[117]
Rubiaceae	*Morinda citrifolia*	Fruit	Extract prevented memory impairment induced by amyloid-β peptide in mice	[118]

Conclusion

Southeast Asia, with its rich tradition of medicinal practices and reliance on natural remedies, offers a diverse array of natural substances with potential memory-enhancing properties. This review has summarized 57 natural substances that originate from, are cultivated in, or are traditionally used in the region, many of which could serve as alternatives to nootropics or have already been incorporated into nootropic formulations. These substances span 32 different families such as the Lamiaceae, Fabaceae and Malvaceae families. The review discusses about the traditional knowledge and scientific evidence related to their memory-enhancing effects While most evidence is derived from animal studies, human clinical studies of effect of rosemary (*S. rosmarinus*) peanut (*A. hypogaea*), arecanut (*A. catechu*) and bacopa (*B. monnieri*) are also discussed. This review also discusses the bioactive compounds of the highlighted substances. However, the specific compounds responsible for memory enhancement and their underlying pharmacological mechanisms in many natural substances remain unclear. Further research is needed to elucidate these mechanisms, identify the compounds responsible for memory enhancement, evaluate their safety profiles and explore the potential of these natural substances as alternatives to existing nootropics.

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