Extended|Longevity

Emophix™

Product Information Sheet

Emophix™ "Emotional Healing Extract" contains **Phytotherapeutic** Extracts of ***Bacopa monniera, Clitoria ternata, Centella asiatica, Withania somnifera, Pannax ginseng and Cinnamomum vera*.** The principal action of **Emophix** is to stimulate the growth of new dendrites in the Amygdala. The purpose of dendritic regeneration in the Amygdala is to allow new neural pathways to be developed in the part of the brain known to control emotions, so as to re-wire the emotional content of the brain by over-writing old hard-wired emotional patterns.

The amygdala is associated with a range of cognitive functions, including emotion, learning, memory, attention and perception. Current views of amygdala function emphasize its role in negative emotions, such as fear, and in the linking of negative emotions with other aspects of cognition, such as learning and memory. *Bacopa monniera* has been demonstrated to have an effect on the dendritic morphology of neurons in the basolateral amygdala, a region that is concerned with learning and memory. Constituents present in *Bacopa monniera* extract have neuronal dendritic growth stimulating properties.

Bacopa monniera (BM), a traditional ayurvedic medicine, is reported to improve learning and memory behaviors in animals and humans. The plant and plant extracts have been extensively investigated for their neuropharmacological effects, and studies have confirmed their nootropic action. The active constituents of the plant facilitate learning and memory-enhancing properties. BM has other potential benefits, such as a facilitatory effect on the capacity for mental retention. BM has been used in ayurvedic medicine and in traditional treatments for a number of disorders, particularly disorders that involve anxiety, intellect and poor memory. Significant antidepressant activity has also been observed.

Clitoria ternatea, The effectiveness of extracts were studied in attenuating electroshock-induced amnesia in rats. Extracts produced significant memory retention. In order to delineate the possible mechanism through which *Clitoria ternatea* elicited the anti-amnesic effects, its influence on central cholinergic activity was studied by estimating the acetylcholine content of the whole brain and acetylcholinesterase activity at different regions of the brain (cerebral cortex, midbrain, medulla oblongata and cerebellum). In vitro and in vivo results suggest the potential of hydroalcoholic extracts of Clitoria ternatea for treatment of cognitive deficit in neurological disorders.

Centella asiatica has been shown to be very useful in improving learning and memory. It is also used as a tonic for promoting brain growth and improving memory. In addition, the plant is used in children with learning difficulties to improve general mental ability and in people suffering from cognitive disorders

Withania somnifera, Also known as Ashwaganda this Ayurvedic herb can boost brain function, lower blood sugar and cortisol levels, and help fight symptoms of anxiety and depression. Several controlled human studies have shown that it can reduce symptoms in people with stress and anxiety disorders

Pannax ginseng

Cinnamomum verum. Contains antioxidants, including polyphenols, phenolic acid and flavonoids

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BASIC RESEARCH

Enhancement of basolateral amygdaloid neuronal dendritic arborization following *Bacopa monniera* extract treatment in adult rats

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OBJECTIVE: In the ancient Indian system of medicine, Ayurveda, *Bacopa monniera* is classified as Medhya rasayana, which includes medicinal plants that rejuvenate intellect and memory. Here, we investigated the effect of a standardized extract of *Bacopa monniera* on the dendritic morphology of neurons in the basolateral amygdala, a region that is concerned with learning and memory.

METHODS: The present study was conducted on 2½-month-old Wistar rats. The rats were divided into 2-, 4- and 6-week treatment groups. Rats in each of these groups were further divided into 20 mg/kg, 40 mg/kg and 80 mg/kg dose groups (n = 8 for each dose). After the treatment period, treated rats and age-matched control rats were subjected to spatial learning (T-maze) and passive avoidance tests. Subsequently, these rats were killed by decapitation, the brains were removed, and the amygdaloid neurons were impregnated with silver nitrate (Golgi staining). Basolateral amygdaloid neurons were traced using camera lucida, and dendritic branching points (a measure of dendritic arborization) and dendritic intersections (a measure of dendritic length) were quantified. These data were compared with the data from the age-matched control rats.

RESULTS: The results showed an improvement in spatial learning performance and enhanced memory retention in rats treated with *Bacopa monniera* extract. Furthermore, a significant increase in dendritic length and the number of dendritic branching points was observed along the length of the dendrites of the basolateral amygdaloid neurons of rats treated with 40 mg/kg and 80 mg/kg of Bacopa monniera (BM) for longer periods of time (i.e., 4 and 6 weeks).

CONCLUSION: We conclude that constituents present in *Bacopa monniera* extract have neuronal dendritic growth-stimulating properties.

KEYWORDS: *Bacopa monniera*; spatial learning; passive avoidance; amygdaloid neurons; dendritic arborization; memory.

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INTRODUCTION

Bacopa monniera (BM), a traditional ayurvedic medicine, is reported to improve learning and memory behaviors in animals and humans.[1-3] The plant and plant extracts have been extensively investigated for their neuropharmacological effects, and studies have confirmed their nootropic action.[1-6] The active constituents of the plant facilitate learning and memory in normal rats and inhibit the amnesic effects of scopolamine, electroshock and immobilization stress.[7,8] BM extracts have been reported to be non-toxic, non-teratogenic and non-mutagenic in rats and monkeys; single and multiple dosing studies in healthy human volunteers have not elicited adverse effects.[9] In addition to its claimed memory-enhancing properties, BM has other potential benefits, such as a facilitatory effect on the capacity for mental retention.[10,11] BM has been used in ayurvedic medicine and in traditional treatments for a number of disorders, particularly disorders that involve anxiety, intellect and poor memory.[3] Significant antidepressant activity comparable to that of imipramine has been observed with the Brahmi extract after five days of oral administration, using a rodent model of depression.[12] Additionally, anticholinesterase activity has been demonstrated.[13]

The amygdala is located deep within the medial temporal lobe, anterior to the hippocampus, close to the tail of the caudate nucleus. The amygdala is structurally diverse and comprises many nuclei. These nuclei are further divided into three major groups: 1) the deep or basolateral group; 2)

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Neuropharmacological Review of the Nootropic Herb *Bacopa monnieri*

Sebastian Aguiar and Thomas Borowski

Abstract

This review synthesizes behavioral research with neuromolecular mechanisms putatively involved with the low-toxicity cognitive enhancing action of *Bacopa monnieri* (BM), a medicinal Ayurvedic herb. BM is traditionally used for various ailments, but is best known as a neural tonic and memory enhancer. Numerous animal and *in vitro* studies have been conducted, with many evidencing potential medicinal properties. Several randomized, double-blind, placebo-controlled trials have substantiated BM's nootropic utility in humans. There is also evidence for potential attenuation of dementia, Parkinson's disease, and epilepsy. Current evidence suggests BM acts via the following mechanisms—anti-oxidant neuroprotection (via redox and enzyme induction), acetylcholinesterase inhibition and/or choline acetyltransferase activation, β-amyloid reduction, increased cerebral blood flow, and neurotransmitter modulation (acetylcholine [ACh], 5-hydroxytryptamine [5-HT], dopamine [DA]). BM appears to exhibit low toxicity in model organisms and humans; however, long-term studies of toxicity in humans have yet to be conducted. This review will integrate molecular neuroscience with behavioral research.

Introduction

Cognitive enhancement typically exacts a toxicological and psychological toll.[1–4] The milieu of nootropic phytochemicals found within *Bacopa monnieri* (BM), primarily triperpenoid saponins called bacosides, exhibit minimal observable adverse effects at standard dosages. BM demonstrates anti-oxidant,[5] hepatoprotective,[6] and neuroprotective[7] activity. Emerging research demonstrates several mechanisms of action—acetylcholinesterase inhibition, choline acetyltransferase activation, β-amyloid reduction, increased cerebral blood flow, and monoamine potentiation.

Herbal medicine is regularly used by 80% of the world population and is increasing in popularity in Europe and North America. [8] In 2008, the National Institutes of Health (NIH) found 4 in 10 adults reported using complementary and alternative medicine (CAM) in the last 12 months, 17.7% of such treatments being herbal medicine.[9] Those with higher education are most likely to use CAM,[10] which may partially reflect the fact that public health insurance used by poor individuals tends not to cover CAM.[11] Herbal medicine tends to be cheaper than pharmaceuticals, albeit less standardized.[12,13] Western biomedicine is in the midst of investigating the potential value of the Eastern pharmacopeia. Of the 150 most used pharmaceutical drugs in the United States, 118 were derived from plants.[14] Traditional medical systems offer a vast library of potentially therapeutic neurological agents,[15] BM is only beginning to undergo rigorous experimental research.

Bacopa monnieri (also known as brahmi, water hyssop, *Bacopa monniera*, and *Herpestis monniera*), is a creeping perennial with small oblong leaves and purple flowers, found in warm wetlands, and native to Australia and India. Commonly found as a weed in rice fields, BM grows throughout East Asia and the United States.[16] The entire plant is used medicinally.

Unlike the potentially addictive and forceful action of widely used psychostimulants, chronic and moderate administration of BM appears to nourish rather than deplete neurons, an action compatible with 1400 years of Ayurvedic study. BM was initially described around the 6th century A.D. in texts such as the *Charaka Samhita, Athar-Ved*, and *Susrutu Samhita* as a *medhya rasayana*–class herb taken to sharpen intellect and attenuate mental deficits. The herb was allegedly used by ancient Vedic scholars to memorize lengthy sacred hymns and scriptures. BM is colloquially called *Brahmi*, after the Hindu creator-god Brahma, especially when combined with other alleged intellect-sharpening herbs like *Centella asiatica* (Gotu Kola). BM is consistently found in the many Ayurvedic preparations prescribed for cognitive dysfunction.

An estimated 3.4 million people are affected by dementia in the United States,[17] most prevalently in the elderly. The elderly population (aged over 65) is expected to double by 2030,

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Pharmacological importance of *Clitoria ternatea* – A review

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Abstract: *Clitoria ternatea* contained tannins, phlobatannin, carbohydrates, saponins, triterpenoids, phenols, flavanoids, flavonol glycosides, proteins, alkaloids, antharaquinone, anthocyanins, cardiac glycosides, Stigmast-4-ene-3,6-dione, volatile oils and steroids. The plant showed many pharmacological effects including antioxidant, hypolipidemic, anticancer, anti-inflammatory, analgesic, antipyretic, antidiabetic, CNS, antimicrobial, gastro-intestinal antiparasitic, insecticidal and many other pharmacological effects. This Review will highlight the chemical constituents and pharmacological effects of *Clitoria ternatea*.

Keywords: *Clitoria ternatea, constituents, pharmacology, pharmacognosy*

I. INTRODUCTION

A large and increasing number of patients in the world use medicinal plants and herbs for health purpose. Therefore, scientific scrutiny of their therapeutic potential, biological properties, and safety will be useful in making wise decisions about their use[1-2]. There are hundreds of significant drugs and biologically active compounds developed from the traditional medicinal plants. Plant showed wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects[3-40]. The preliminary phytochemical screening showed that *Clitoria ternatea* contained tannins, phlobatannin, carbohydrates, saponins, triterpenoids, phenols, flavanoids, flavonol glycosides, proteins, alkaloids, antharaquinone, anthocyanins, cardiac glycosides, Stigmast-4-ene-3,6-dione, volatile oils and steroids. The plant showed many pharmacological effects including antioxidant, hypolipidemic, anticancer, anti-inflammatory, analgesic, antipyretic, antidiabetic, CNS, antimicrobial, gastro-intestinal antiparasitic, insecticidal and many other pharmacological effects. This Review will highlight the chemical constituents and pharmacological effects of *Clitoria ternatea*.

Plant profile:

Synonyms:

Clitoria albiflora Mattei, *Clitoria bracteata* Poir., *Clitoria mearnsii* De Wild., *Clitoria tanganicensis* Micheli, *Clitoria zanzibarensis* Vatke[41].

Taxonomic classification:

Kingdom: Plantae; **Subkingdom**: Viridaeplanta; **Infrakingdom**: Streptophyta;
Division: Tracheophyta; **Subdivision**: Spermatophytina; **Infrodivision**: Angiospermae; **Class**: Magnoliopsida; **Superorder**: Rosanae; **Order**: Fabales;
Family: Fabaceae; **Genus**: Clitoria L.; **Species**: *Clitoria ternatea*[42-43].

Common names:

Arabic: Mazerion Hidi, Baslat el-Zuhoor; **Bengali** : Aparajita, **Chinese:** die dou**; English:** blue-pea, bluebellvine, butterfly-pea, cordofan-pea, Darwin-pea**; French:** honte**; German:** blaue Klitorie**; Hindi** : Aparajita, **Portuguese:** clitória-azul, clitória; **Punjabi**: Koyal; **Sanskrit**: Girikarnika, Vishnukranta; **Spanish:** conchitas papito, azulejo, zapatico de la reina, zapotillo; **Swedish:** himmelsärt; **Tamil**: Kakkanam and **Telugu** : Dintena[41,43].

Distribution:

The plant originated from tropical Asia and later was distributed widely to **Africa**: (Chad, Djibouti, Ethiopia, Somalia, Sudan, Sudan, Kenya, Tanzania, Uganda, Burundi, Cameroon, Gabon, Sao Tome, Zaire, Benin, Cote D'Ivoire; Gambia, Ghana, Guinea, Guinea-Bissau, Niger, Nigeria, Senegal, Sierra Leone, Togo, Angola, Malawi, Mozambique, Zambia, Zimbabwe and South Africa; **Asia:** Madagascar**,** Saudi Arabia, Yemen, Iran, Iraq, China Taiwan, Bangladesh, Bhutan, India, Nepal, Pakistan, Sri Lanka, India, Maldives, Cambodia, Laos; Myanmar, Thailand, Vietnam, Indonesia, Malaysia, Philippines and Singapore; **Australia**; **North America:** USA and Mexico; **Northwestern Pacific:** Guam, Northern Mariana Islands, Palau, **South-Central Pacific:** French Polynesia - Society Islands; **Southwestern Pacific:** Fiji, New Caledonia, Samoa, Solomon Islands, **Southern America:** Antigua, Barbuda, Aruba, Bahamas, Barbados, Cayman Islands, Cuba, Dominica, Dominican Republic, Guadeloupe, Haiti, Jamaica, Martinique, Montserrat, Netherlands Antilles, Puerto Rico, St. Kitts and Nevis, St. Vincent and Grenadines, Virgin Islands (British), Virgin Islands (U.S.), French Guiana,

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RESEARCH ARTICLE

Regeneration of dendritic cells in aged mice

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Age-related thymic involution causes a decreased output of thymocytes from the thymus, thereby resulting in impairment of T cell-mediated immunity. While alterations in the T cell and non-haematopoietic stromal compartments have been described, the effects of thymic involution on thymic dendritic cells (DC) are not clearly known. Thymic DC play an essential role in shaping T cell-mediated immune responses by deleting self-reactive thymocytes to establish central tolerance and by inducing regulatory T-cell (Treg) development. It is therefore important to assess the prevalence of and alterations to thymic DC with age, as this may impact on their function. We assessed the numbers and proportions of the three distinct subsets of thymic DC in ageing mice, and showed that these subsets are differentially regulated. This is expected as thymic DC subsets have different origins of development. We further assessed the responses of thymic DC in a regenerative environment, such as that induced by sex-steroid ablation (SSA), and clearly showed that, consistent with global thymus regrowth, all three DC populations increased in numbers and regained their relative proportions to thymocytes after an initial lag period. These findings are important for the clinical translation of thymic regenerative approaches, and indicate that SSA facilitates the maintenance of critical processes such as negative selection and Treg induction through promoting thymic DC regeneration.
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Keywords: ageing; dendritic cells; thymic regeneration

INTRODUCTION

The thymus has a central role in the deterioration of the immune system with age due to its natural involution.[1] Some thymic decline is initially apparent from as early as the first year in humans, but then thymus undergoes more pronounced degeneration from puberty such that by ~25 years of age, the thymus has decreased to approximately 50% of its size at birth progressing through to ~10% capacity by the fifth and sixth decades.[2] While the mechanisms of thymic involution have not been precisely defined, there is a clear correlation with the influence of sex steroids, the removal of which reverses thymic atrophy in animal models.[1,3–8] The progressive decrease in thymus size with age is associated with a loss in thymic epithelial cells and a concomitant decrease in thymopoiesis[9] leading to a reduced thymic output of naive T cells.[8,10–12] Although homeostatic proliferation ensures that the number of T cells in the periphery is maintained, the T-cell receptor repertoire is decreased due to greater clonal expansion of fewer thymic exported T cells.[13,14] The T-cell population becomes disproportionately high for memory T cells as the naive T cells become progressively exposed to environmental antigens.[15–17] Thus, attrition of the thymus contributes to the impairment of T cell-mediated immunity seen in the aged population and in patients recovering from chemotherapy or suffering from immunoablative diseases such as HIV. Full immune recovery is dependent on high thymic output of naive T cells to replenish the peripheral pool.[18] Consequently, there is considerable clinical interest in developing strategies to improve immune reconstitution, one of which is to regenerate the involuted aged or damaged thymus (reviewed in Ref. 19).

The inhibition of sex steroids has a dramatic impact on reversing the age-related degeneration of the thymus. Clinically, a reversible reduction in sex steroids is achieved by the agonist variants of luteinising hormone releasing hormone (reviewed in Ref. 20). In mouse models sex-steroid ablation (SSA) can be achieved through surgical or chemical castration (reviewed in Refs. 4 and 20–22), which in both cases results in the regeneration of the thymus and thymopoiesis, thereby increasing the number of naive T cells and providing a more diverse T-cell receptor repertoire in the periphery. Following SSA in male mice, there was an improvement in immune reconstitution in young (4–6 weeks), adult (3 months), middle-aged (9 months) and aged (18–24 months) mice in several immunocompromised models.[1,8,23,24] Increased proliferation was evident in early thymocyte subsets such that by 14 days post-castration, the aged thymus resembled a young thymus in cellularity.[8,23–25] SSA also induces changes outside the thymus with increases in immature cell types and lymphoid progenitors, such as haematopoietic stem cells and $Lin^{-}Sca\text{-}1^{+}c\text{-}Kit^{+}$ cells, which are evident in the bone marrow. This leads to an increase in all immature B-cell subsets[23,24] and also likely contributes to the increase along the developmental pathway of thymocytes.[8,24,26]

Little is known about the response of dendritic cells (DC) in this environment. It is important to determine potential changes in the distribution or activation phenotype of DC as these cells play an important role in thymic education, particularly in negative selection and the induction of T regulatory cells (Tregs).[27,28] These processes

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Review Article

Recent Updates in Neuroprotective and Neuroregenerative Potential of *Centella asiatica*

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Abstract

***Centella asiatica*, locally well known in Malaysia as pegaga, is a traditional herb that has been used widely in Ayurvedic medicine, traditional Chinese medicine, and in the traditional medicine of other Southeast Asian countries including Malaysia. Although consumption of the plant is indicated for various illnesses, its potential neuroprotective properties have been well studied and documented. In addition to past studies, recent studies also discovered and/or reconfirmed that *C. asiatica* acts as an antioxidant, reducing the effect of oxidative *stress in vitro and in vivo*. At the in vitro level, *C. asiatica* promotes dendrite arborisation and elongation, and also protects the neurons from apoptosis. In vivo studies have shown that the whole extract and also individual compounds of *C. asiatica* have a protective effect against various neurological diseases. Most of the in vivo studies on neuroprotective effects have focused on Alzheimer's disease, Parkinson's disease, learning and memory enhancement, neurotoxicity and other mental illnesses such as depression and anxiety, and epilepsy. Recent studies have embarked on finding the molecular mechanism of neuroprotection by *C. asiatica* extract. However, the capability of *C. asiatica* in enhancing neuroregeneration has not been studied much and is limited to the regeneration of crushed sciatic nerves and protection from neuronal injury in hypoxia conditions. More studies are still needed to identify the compounds and the mechanism of action of *C. asiatica* that are particularly involved in neuroprotection and neuroregeneration. Furthermore, the extraction method, biochemical profile and dosage information of the *C. asiatica* extract need to be standardised to enhance the economic value of this traditional herb and to accelerate the entry of *C. asiatica* extracts into modern medicine.**

Keywords: *antioxidant, neuroprotective, neurological disease, neuronal injury, pegaga*

Introduction

The nervous system, consisting of the brain, spinal cord, and peripheral nerves, is made of complex and specialised structures which are vulnerable to various diseases and injury that reduce sensorimotor and cognitive functions, and may also be the cause of life-threatening problems in acute cases. Unfortunately, spontaneous regeneration and healing processes occur very minimally in damaged tissues due to their high complexity. Our team of researchers at the Tissue Engineering Centre, Universiti Kebangsaan Malaysia has been conducting research on the regeneration of various tissues, and studies on nerve regeneration for development of cell and tissue therapies have been going on for almost eight years (1,2). We have identified various cell sources, ranging from stem cells to adult nerve cells, and developed various scaffolds, ranging from biological tissue to synthetic hollow tubes, to enhance in vitro and in vivo nerve regeneration (3–6). Realising the historical nature of medicinal herbs, we were attracted to scrutinise the pharmacological effects of herb extracts in synergy with the provided cells and scaffolds to further enhance nerve regeneration, and also to improve the utilisation of tissue-engineered nerve grafts and cell therapy in clinical applications for nerve degeneration and injury.

It has been reported that there are 250 000 plant species on the earth, and approximately 5

