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Review Article

Medicinal Importance of *Bacopa monnieri* (L.) Pennel

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ABSTRACT

This review highlights the medicinal importance of Bacopa monnieri. Bacopa monnierawas distributed in the warmer and wetlands regions of the world. It was widely used in traditional medicine to treat various complains. Bacopa monnieracontained alkaloid brahmine, nicotinine, herpestine, bacosides A[3-(α-L-arabinopyranosyl)-O-β-D-glucopyranoside-10,20-dihydroxy-16-keto-dammar-24-ene], triterpenoid saponins , saponins A, B and C, betulinic acid , D-mannitol, stigmastanol, β-sitosterol, stigmasterol. and pseudojujubogenin glycoside. The present review summarizes our current knowledge of pharmacological actions, preclinical and clinical studies, major bioactives, reported mechanisms of actions, clinical efficacy, safety and the possibility of interactions of the herb with the conventional drugs.

Key words: *Brahmi, Antioxidant, Medicinal plant, Micropropagation.*

INTRODUCTION

According to recent World Bank report; "Medicinal Plants: Rescuing a global heritage", a large number of medicinal plant are being over harvested and could soon become extinct, unless, stringent conservation measures are introduced by developing countries. Many of these plants have been used since ancient times to treat a variety of ailments but during the past few years, there has developed a booming world trade in plant remedies, leading to over harvesting. The report adds, unless swift action is taken, it warns more plants will be gone forever, more than four billion people in the developing world depend heavily on natural medicinal for their daily health and that the global trade in medicinal plants is now worth in excess of one trillion, the need for better conservation is beyond question, the report maintains with the exception of China and India which are the world's biggest suppliers of herbal medicines, most developing countries invest little or nothing in the conservations, cultivation and use of the medicinal plants. Other cash crops get millions of dollars in research support but the production of "these exceptionally promising generations of income and well being" are left to languish with the result of the many are in danger of extinction.

The use of traditional medicines and medicinal plants in most developing countries as a normative basis for maintenance of good health has been widely observed.

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Further an increasing reliance on the use of medicinal plants in the industrialized societies has been related to the development of several drugs and chemotherapeutics from plant species as well as from traditionally used rural herbal preparations. Herbal remedies have attained much more popularity in the treatment of minor ailments, due to increasing awareness of personal health maintenance through natural products. Indeed, the market and public demand has been so great that there is a great extinction risk to many medicinal plants and obviously the loss of genetic diversity.

To cope up with alarming situation the recent exciting developments in biotechnology have come as a boon. One of them is the use of plant tissue culture technique. Most of the plant raised through seeds are highly heterozygous and show great variations in growth, habit and yield and may have to be discarded because of poor quality of products for their commercial release. Likewise, majority of the plants are not amenable to vegetative propagation through cutting and grafting, thus limiting multiplication of desired cultivars.

In recent years, tissue culture has emerged as a promising technique to obtain genetically pure elite populations under *in vitro* conditions rather than have indifferent populations. Tissue culture has now become a well established technique for culturing and studying the physiological behavior of isolated plant organs, tissues, cells, protoplasts and even cell organelles under precisely controlled physical and chemical conditions. *In vitro* propagation also called micropropagation is in fact the miniature version of conventional propagation, which is carried out under aseptic conditions.

Mass multiplication of disease free planting material is a general problem. In this regard the micropropagation holds significant promise for true to type, rapid & mass multiplication under disease free conditions.

Global overview of Medicinal plants

Plants, since time immemorial, have been used globally across the varied cultures throughout the known civilizations as a valuable and safe natural source of medicine and agents of therapeutic, industrial and environmental utilities. According to the World Health Organization, over 80% of the world's population or 4.3 billion people rely upon such traditional plant based systems of medicine to provide them with primary health care.

Allopathic medicine too owes a tremendous debt to medicinal plants: one in four prescriptions filled in a country like the United States is either a synthesized form of or derived from plant materials. Even from the earliest trade data available, it is clear that the global market for medicinal plants has always been very large. It is only during the last decade that the real significance of the medicinal plants sector has begun to be realized.

International market of medicinal plants is reported to be over 62 billions US dollars per year during 2000-2001, which is growing at the rate of 7% annually. The botanical retail market, inclusive of herbs and medicinal plants, in USA, is estimated at approximately US$1.6 billion annually. It is estimated that Europe annually imports about 400,000 tones of medicinal plant material with an average market value of US$1 billion from Africa and Asia. A growing awareness of this new contributor to the foreign exchange reserves of several national treasuries is beginning to emerge. To satisfy the growing market demands, surveys worldwide are being conducted by the pharmaceutical industries and research organization to unearth new plant sources as herbal remedies, medicines and biomolecules.

Status of Medicinal plants in India

Medicinal plants as a group comprise approximately 8000 species and account for about 50% of all the higher flowering plant species of India. Millions of rural mass use medicinal plants. In recent years the growing demand for herbal products has led to a quantum jump in volume of plant material traded within and outside the country. An estimate of the EXIM Bank projects international market of medicinal plants

related trade over US $ 60 billion per year that is growing at a rate of 7% per year.

India's surface land has been grouped into ten distinct zones and these are further divided into 25 biotic provinces and 426 biomes. The forest areas of these bio-geographic zones/provinces are classified into 16 major forest types and more than 200 subtypes.

A macro analysis of the distribution of medicinal plants shows around 70% of India's medicinal plants are found in tropical and subtropical forests and less than 30% are found in the temperate and high altitude forests. The medicinal plants species belong to a wide range of habits/life form viz. trees, herbs, shrubs, lianas, and woody climbers. Habit wise analysis carried out so far indicates that nearly one third of these botanical entities are trees and around the same proportion consists of shrubs and woody climbers. The remaining one third are herbs and twiners. Very small proportions of the medicinal plants are lichens, ferns, algae etc; the majority of the medicinal plants are higher plants.

The need of the hour, then, is to replace India's participation in the expanding global market, in light of the interest of all the stakeholders who are affected and who play a role in this sector. There is a need to collect all the available information regarding medicinal plants development in the country in order to obtain a comprehensive overview, which will provide the necessary insight for coordinated and effective action. Such an overview could form the basis of a renewed development of India's medicinal plants sector, and a strategic exploitation of her comparative advantage in the global market on a sustainable and equitable basis.

Important medicinal plants in India

The Indian system of medicine particularly Ayurveda, Siddha, Unani and Homeopathy largely use plant-based materials, minerals, metals, marine and products of animal origin. The domestic market of Indian system of medicine and Homeopathy is of order of Rs 4000 crores which is expanding day by day. The Ayurveda drug market alone is of the order of Rs 3500 crores, besides this there are demands from food supplements and cosmetics. However, the sector is not well organized and needs special attention. Hence, the National Medicinal Plants Board was set up under the ministry of Heath and Family welfare, Govt. of India during 2000 and the board has initially identified 31 species of importance. In a report to the Scientific Advisory Committee to the cabinet (SAC-C), Govt. of India, Technology Information, Forecasting and Assessment Council (TIFAC) has mentioned 45 medicinal plant species and specifically recommended 7 plants for immediate attention during 2001-2005. They are as follows-

1. *Aloe vera* (Ghrita Kumari)
2. *Bacopa monnieri* (Brahmi)
3. *Centella asiatica* (Mandukparni, Gotukola),
4. *Rawolfia serpentine* (Sarpagandha),
5. *Catharanthus roseus* (Periwinkle)
6. *Taxus bacata*

Bacopa monnieri is believed as one of the most important herbs. The whole series of traditional medicine plants, which have been in use for thousands of years. *B. diffusa* is a good remedy in traditional medicine as in used to treat skin diseases, leprosy, epilepsy, eczema, asthma, hoarseness of the voice, and diseases of the nervous system[47].

History of Bacopa

In the folklore of Indian medicine, certain herbs have been used traditionally as brain or nerve tonics. One of the most popular of these used in neurotonics is Bacopa monnieri, a small, common, amphibious plant growing in marshy areas throughout the Indian subcontinent. Bacopa is also called Brahmi, a name derived from Brahma, the creator god of the Hindu pantheon of deities. It is legendary for its diversity of usage. In the Ayurvedic Materia Medica, Bacopa has been recognized for its brain- enhancement characteristics.

It is said that the use of Bacopa for memory enhancement goes back 3000 years or more in India, when it was cited for its medicinal properties, especially the memory- enhancing capacity, in the Vedic texts Athar-Ved Samhita (3:1) of 800 B.C. and in Ayurveda.

Back before written language, ideas and cultural values were transmitted by epic hymns or poems that were committed to memory and transmitted orally from one generation of Brahmins (the highest class of priests) to the next Bacopa is reputed to have played a role in increasing the ability to memorize the great epic poems, possibly helping new generations to learn from the past and not make the same mistakes - a value spoken of by philosopher George Santayana when he wrote, "Those who cannot remember the past are condemned to repeat it."

Taxonomy

Scientific name: *Bacopa monnieri* L. Penn

Family: Scrophulariaceae

Common names: Sanskrit – Nir Brahmi, Hindi – Brahmi, Bengali – Brahmi sak, Marathi/Tamil/Malayalam – Nir brahmi, Kannada – Niru brahmi

Habitat and Botanical description

Bacopa monnieri has originated in India. A genus of spreading herbs, commonly growing in damp and marshy places throughout India, ascending up to an attitude of 1,320 m, a small creeping, glaburous, succulent, herb rooting at nodes. Stem soft obtuse- angular, branches ascending, leaves are sessile, opposite decussate, succulent, obovate or oblanceolate in shape , short petiolate, 0.6-2.5 cm in size, flowers solitary axillary, blue or white in color with purple veins, campanulate, pentamerous, capsules ovoid[30]. Flowers and fruits appear in summer. Whole plant forms the medicinally useful part.

Propagation and agronomy

Bacopa monnieri spreads by producing new plants on above ground runners. The new plants can be separated from the parent plant once they have taken root. The natural regeneration of this herb is hampered by death of seedlings at 2-leaved stage and specific habitat (marshy areas) requirements. Bacopa seems to be poor competitor and so it can colonize open spaces only[64]. A field trial involving five Indian accessions of Bacopa monnieri was conducted during 1997 to 1998, at Lucknow, Uttar Pradesh, India, to standardize the cultivation procedure for the domestication of this medicinal herb. The accessions monitored for growth and bacoside-A yields over 18 months, could be maintained as perennials, but growth properties were sensitive to the growing season. Loss of shoot biomass occurred in winter (December-February) and the growth rate was higher in the monsoon season (July-September) than in summer (March-June). Bacoside-A content of herb was high from September through March and in June. Suitable harvest times for high yields of bacoside-A were June and September through November. An accession from Guwahati in Assam state of India yielded more bacoside-A than all other accessions.

Medicinal uses

In India the plant is used for all sorts of skin problems- eczema, psoriasis, abscess, ulcerations- it is said to stimulate the growth of skin, hair and nails. Indian Pennywort is also used for chronic rheumatism often as an ointment. In Pakistan, the herbal drug, Brahmi-buti, is used to treat skin diseases, leprosy, epilepsy, eczema, asthma, hoarseness of the voice, and diseases of the nervous system[47].

According to scientists at the Central Drug Research Institute in Lucknow, India, certain "memory chemicals" in Bacopa, called bacosides A and B, help repair damaged neurons by enhancing proteins involved in the regeneration of neural-cell synapses[34]. These are the relay stations of the brain that facilitate the transmission of neural impulses. Thus Bacopa can be viewed as a neural nourisher, restoring depleted synaptic activity and leading to enhanced memory function.

In scientific studies, it has been shown to exert a remarkable and unique effect on neurotransmitters. Bacopa may even be able to revitalize intelligence. Among its many other

applications, Bacopa has reportedly been effective in reducing anxiety levels, thereby allowing for further improvement of brain functioning and elevated mental performance. It is also believed to help stabilize the brain waves of epileptics. Bacopa is recognized as a treatment for asthma, bronchitis, and hoarseness. In other parts of the body, it has been used successfully as a remedy for rheumatism, for diarrohea, and as a diuretic (increasing urinary flow).

Bacopa also has important antioxidant properties and acts as a metal chelator, removing excess damaging metals from the blood, thus limiting the propagation of free radicals. Perhaps most intriguing of all, in human studies Bacopa appears to increase a child's exploratory behavior, improve visual motor performance, and exercise a positive effect on recall and reaction time.

Chemistry

Plant contains two saponins, bacoside A and B. In addition to the bacosides, Bacopa contains a wide variety of medically active substances, including stigmasterol, sapogenins, and flavonoids. Other compounds include triterpenoid saponins. Bacopa also contains D-mannitol, betulic acid, beta-sitosterol, octacosane, nicotine, and amino acids such as alpha-alanine, aspartic acid, glutamic acid, and serine. Alkaloids such as Brahmines, Herpestine and a mixture of three alkaloids were reported from the leaves of this plant. The carbohydrate mostly of bacoside A was shown to be arabinosyl glucose with the arabinose unit as the terminal sugar. Bacoside B was found to be dextorotatory where as bacoside A was laevo rotatory. The haemolytic action of bacoside B is twice that of bacoside A (Report on Herbal industry, pp : 37 –41). This is because of the differences in the configuration of the carbohydrate parts. Bacoside a Yields bacogenins A1, A2, A3 and A4 upon hydrolysis. The other chemical constituents of the plant includes bacoside A1, hersaponin, betulinic acid, stigmasterol, b sitosterol and stigmastenol.

Medicinal properties

Central nervous system Bacopa meditates the GABAergic system. Gamma-aminobutyric acid is an inhibitory neurotransmitter that has been shown to possess anticonvulsive, antinociceptive (prevention of pain due to hypersensitive nerve endings), locomotor, and sedative effects. Because Bacopa also has all these properties, it is reasonable to speculate that a similar mechanism of action explains its effects on the brain and the body.

Antidepressant activity

The standardized extract was reported earlier to have significant anti-oxidant effect, anxiolytic activity and improve memory retention in Alzheimer's disease. Presently, the standardized methanolic extract of Bacopa monniera (bacoside A) was investigated for potential antidepressant activity in rodent models of depression. The effect was compared with the standard antidepressant drug imipramine. The Bacopa extract when given in the dose of 20 and 40 mg/kg, orally once daily for 5 days was found to have significant antidepressant activity in forced swim and learned helplessness models of depression and was comparable to that of imipramine. Attention - deficit disorder Another application comes from clinical reports of Bacopa's use for attention-deficit hyperactivity disorder (ADHD) in children. In a study conducted at BRD Medical College at Gorakhpur, 36 children in the 8-10-year age group were selected for a double-blind, randomized trial. While 19 were given 50 mg of Bacopa twice daily, 17 others received placebo. After 12 weeks of treatment, the children were subjected to a battery of specialized tests. The data revealed a significant improvement in the areas of sentence repetition, logical memory, and pair-associative learning (matching things that go together; e.g., "test" and "grade") in all 19 ADHD children who took Bacopa. Anxiety and Blood pressure Singh and Singh reported that for four weeks, 35 patients were treated for anxiety neurosis. After treatment, they were assessed for clinical anxiety levels,

maladjustment level, mental fatigue rate, and immediate memory span. In those patients receiving Bacopa anxiety levels were lowered by about 20%. Maladjustment was

significantly lower than its corresponding pretreatment value. Mental fatigue, as determined in total daily work output, was lower. Immediate memory-span scores were significantly increased.

Antioxidant

It helps prevent induced lipid peroxidation[65]. Its protective capacity was found to compare favorably to the effects of the chelating agent EDTA and to those of the natural antioxidant vitamin E. The results suggest that Bacopa is a potent antioxidant. It has been suggested that its role in memory enhancement may be due in part to its ability to increase brain circulation by inhibiting oxidative damage in the brain. It also enhances serotonin levels in the brain.

Antimicrobial

The phytochemicals betulinic acid, wogonin and oroxindin isolated from the aerial parts of Bacopa monnieri showed significant antifungal activity against the two fungi Alternaria alternata and Fusarium fusiformis.

Status of *Bacopa monnieri*

According to NMPB, annual demand of Bacopa during the year 2004-2005 is 6621.8 tons with an annual growth rate of 7% annually. This requirement is rising rapidly in view of the popularity of the Bacopa based drugs. In view of the wider market demand, there is need to conserve the wild stocks of B. monnieri. (http://nmpb.nic.in/) With the release of new drugs like Memory Plus in the market, there is going to be over exploitation of the natural populations of B.monneri that must meet the present requirement of 0.1 million quintal/year of the herb. There is thus an immediate need for assessing the natural populations, developing protocols for micro propagation, regeneration and agronomical practices. The characteristics of rapid vegetative growth, available morphological variation and short sexual life cycle raise the possibility of using Bacopa monnieri in the developmental studies related to bioprospection, morphogenesis and secondary metabolism[30].

A collection of 24 B. monnieri accessions from different agro-climatic zones of India and an introduction from Malaysia maintained in the field genebank at CIMAP was analyzed for RAPD variation. Among the 40 random primers tested, 29 primers generated one or more polymorphic bands. The number of polymorphic bands generated was primer dependent, ranging from a minimum of 2 to a maximum of 8. Similarity matrices were generated from the RAPD data on the basis of Nei's estimates of similarity indices and dendrograms were constructed based on UPGMA clustering. All the accessions were found to be in the range of 0.8-1.0 of similarity, which is indicative of a narrow genetic base among the various accessions with a medium level of polymorphism.

It was possible to differentiate individual accessions, showing differences in morphological and growth properties at DNA level. The observed low levels of genetic variation were attributed to interplay of sexual and vegetative modes of reproduction and similarity of local environments in habitats of B. monnieri.

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