IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A Review on *Bacopa monnieri*: A Promising Medicinal Plant with Potential Glycosylation and Therapeutic Properties

Shalinee Maddheshiya[1], Sumit kumar Pandey[1] Dr. Rakesh kumar shukla[2], Dr.Jyoti Prakash[1]

1. Amity Instiute of Biotechnology, Amity University Lucknow, India.
2. CSIR- Central Institute of Medicinal and Aromatic Plants, Lucknow, India.

Abstract -

The use of medicinal plants for therapeutic purposes dates back to ancient times, with *Bacopa monnieri,* also known as Brahmi, being one such plant with a long history of traditional usage in Ayurvedic medicine. *Bacopa monnieri* has gained attention for its potential cognitive-enhancing properties, including memory improvement and stress reduction. This review explores the chemical constituents, medicinal uses, and potential mechanisms of action of *Bacopa monnieri*, with a specific focus on the role of glycosylation in its therapeutic properties. Glycosyltransferases, enzymes involved in glycosylation processes, play a crucial role in the synthesis of various metabolites in plants and have been identified as potential targets for understanding the biological activities of *Bacopa monnieri.* The glycosylation reactions in *Bacopa monnieri* contribute to the formation of natural glucosides and may be involved in maintaining cellular homeostasis, regulating plant development, and enhancing defense mechanisms under stressful conditions. Furthermore, glycosyltransferases can modify the bioactivity, stability, solubility, and toxicity of plant compounds, potentially enhancing their therapeutic potential. The classification and functional characterization of glycosyltransferases provide insights into their roles in plant growth, development, and response to the environment. Future research on glycosylation processes and glycosyltransferases in *Bacopa monnieri* may unravel novel therapeutic applications and contribute to the development of glycoside-based drugs.

Keywords - *Bacopa monnieri* , Glucosyltransferase, Glycosylation, Bacosides, Glucosides.

INTRODUCTION

Since ancient times, several plants have been used for therapeutic purposes. Due to the existence of natural chemicals, medicinal plants are the source of molecules with therapeutic qualities. Before the development of modern medicine, people used herbal remedies, but the majority of plants still exist today about which it is unknown the pharmacological foundations of their activities. Ayurvedic traditional medicine has employed the plant *Bacopa monnieri* for ages. It also goes by the name Brahmi. Certain brain chemicals that are important in thinking, learning, memory, etc. may be increased by *Bacopa*. Additionally, it can protect brain cells against harmful chemicals linked to Alzheimer's disease. The Indian medicinal plant *Bacopa monnieri* is an excellent source of dietary antioxidants that can protect the ageing brain from oxidative stress and cognitive decline [1]. Multiple studies have indicated that the older group gained most from the standardised Bacopa extract's improvement in mental performance.

The beneficial qualities of *B. monnieri* is based on the existence of triterpenoid saponins called bacosides. *Bacopa monnieri* contains flavonoids, alkaloids, betulic acids, sterols such as beta -sitosterol and stigmasterol along with sponins. Due to presence of active compounds, Bacopa monnirei has been used as nootropic digestive system and is employed for improving respiratory function. *Bacopa monnieri* are widely used in various commercial production due to its memory enhancing properties. A formulation ‘Bacosides Enriched Standardized Extract of Bacopa’’ marketed under the brand name KEEN MIND has been formulated by Central Drug Reasearch Institute, Lucknow along with this is widely used as memory enhancing drug .

Fig - Mature *Bacopa* plant with flower and stem of *Bacopa*

Glycosylation reactions hold a great biological significance in both prokaryotes as well as eukaryotes. The coordinated activity of several enzymes, through the glycosyltransferases (GTs), is necessary for these processes. A developing chain of oligosaccharides, a lipid, or a protein can get the sugar moiety from an active nucleotide-sugar through the use of glycosyltransferases. Glycosylation is one of many key that plant use a variety of methods to maintain metabolic equilibrium and to synthesize several thousand different low molecular weight metabolites. Glycosylation results in the formation of several natural glucosides and are thought to be produced as the last stage in the secondary metabolites prroduction.

In this way, glycosyltransferases may have a significant role in preserving cell homeostasis as well as regulating plant developments, advancement, and defence reaction under stressed conditions.

REVIEW OF LITRATURE

Bacopa monnieri –

Bacopa monnieri frequently referred to as 'Brahmi' relates to the Scroophuariaceae (figwort or snapdragon) family. The Hindu pantheon's mythical "creator," Brahama, is the source of the name "Brhami." Since the brain serves as the primary organ for creative activities, Brahmi refers to any substance that enhances brain function.It is a little herb, and its flowers are light purple in shade. Furthermore, this plant develops in sandy and moist swampy environments. Plants have uncomplicated, opposite, fleshy leaves with minor veining. Summer is often when blooms and fruits appear, and stem segments and seeds are used to spread them around. 'lemon' scent are produced by the crushed leaves of Brahmi. The plant is distributed in India, Pakistan, Afghanistan, Nepal, Sri Lanka, Africa and Australia. *B. monnieri* is cultivated for medicinal purposes, around 40,000 to 50,000 kg per hectare annualy produced. The medicinal plant was mentioned in Ayurvedic literature around 800 BC, and the Charaka Samhita text lists it as a form of treatment for mental illnesses.The Indian Ayurvedic medical system frequently utilises *B.monnieri*, sometimes known as "the thinking person's herb," as an effective nervine boost to enhance memory, brain, and thinking abilities[1]. This plant is also used to cure asthma, kidney problems, water retention, and to clear the blood. In Ayurveda, the utilization of the *B.monnieri* is not very restricted as a brain tonic only however,to also heal the gastrointestinal disturbances, habitual abortions, high blood sugar (due to anxiety), epilepsy. A medicinal product called "Memory Plus" that contains standardised Brahmi plant extract has been sold in India. According to a sector assessment by the Export Import Bank of India, *B. monnieri* was ranked second in the priority list of medical plants based on their medicinal plant's commercial worth and potential for further research and development. It was predicted that the manufacturing plant would need about 12,700 dry tonnes of material annually, which would cost around $15 billion.

History of *Bacopa monnieri*

The past of *Bacopa monnieri* can be attributed to ancient India, where it was utilized as a medicinal plant for over 3000 years. It was first mentioned in the Atharva Veda, one of the four sacred texts of Hinduism, as a herb that can improve memory and cognitive function. It was also used as a tonic for bettering general health and vitality. Traditional medical systems all around the world have long used *Bacopa monnieri*, commonly known as Brahmi, water hyssop, or herb of grace. It is native to wetlands and muddy shores in regions such as India, Nepal, Sri Lanka, and Southeast Asia

In India, in Ayurvedic medicinal system *Bacopa monnieri* has been utilised for many years. It is among the most commonly used herbs in Ayurvedic medicine, where it is known as Brahmi. In the Ayurvedic medicinal system,

Bacopa monnieri has been utilised to improve cognitive function, reduce anxiety, and treat a variety of other health conditions. It is believed to be a powerful brain tonic and is often used to improve memory and concentration. *Bacopa monnieri* is also believed to have a calming effect on the mind and is used to reduce stress and anxiety.

Bacopa monnieri has also been used in traditional medicinal systems in other parts of the world. In Nepal, the herb is known as Jal Brahmi and is used to treat a variety of health conditions, including epilepsy, asthma, and ulcers. In Sri Lanka, the herb is known as Kikirindiya and is used to treat a number of illnesses, such as fever and respiratory infections

The use of *Bacopa monnieri* in traditional medicine systems is accepted by a long history of informal proof and observations. However, modern scientific research has also begun to shed light on the potential medicinal properties of the herb. Studies have suggested that *Bacopa monnieri* may improve cognitive function, reduce stress and anxiety, and have antioxidant properties.

In addition to its traditional medicinal uses, *Bacopa monnieri* is also used in cooking in some parts of the world. In India, the herb is often used as a flavoring agent and is added to curries and chutneys. The plant's leaves are also used to prepare teas and extracts in traditional medical treatments.

Overall, *Bacopa monnieri* has a rich history of use in traditional medicinal systems throughout the world. Its potential medicinal properties, as well as its use in cooking, make it an important plant in many cultures. The continued study of *Bacopa monnieri* and its potential uses in modern medicine and industry will likely shed new light on this remarkable plant.

Fig- Subculture of *Bacopa monnieri*

Medicinal usage:

Brahmi, also known as *Bacopa monnieri*, has been used for thousands of years in traditional medical systems to treat a number of diseases.. Modern scientific research has begun to uncover the potential medicinal properties of this herb, confirming some of the traditional uses and revealing new ones.

Fig - Products available in market

Cognitive Function and Memory Enhancement

Bacopa monnieri is perhaps best known for its potential to enhance cognitive function and improve memory. Numerous studies have suggested that the herb may have a good effect on cognitive performances, including memory consolidation as well as recall, attention, and learning. These effects may be due to the plant's ability to increase the production of certain neurotransmitters, such as acetylcholine, which are important for cognitive function.[2]

Anxiety and Stress Reduction

Bacopa monnieri has also been shown to have anxiolytic and stress-reducing effects. In one study, participants who took *Bacopa monnieri* supplements for 12 weeks showed anxiety levels were substantially lower than in the unaffected group. Another study found that *Bacopa monnieri* may have a calming effect on the mind, reducing stress and improving mood.

Anti-Inflammatory and Antioxidant Effects

It has been demonstrated that *Bacopa monnieri* contains anti-inflammatory and antioxidant properties, which may make it effective for treating a range of medical disorders. According to one study, the herb's anti-inflammatory qualities may be comparable to those of NSAIDs (non-steroidal anti-inflammatory drugs). Additionally, it has been demonstrated that *Bacopa monnieri* possesses powerful antioxidant qualities that can support in preventing cell deterioration caused by free radicals.

Neuroprotection

It has been found that *Bacopa monnieri* possesses neuroprotective properties, which may contribute in preventing age-related cognitive decline and neurodegenerative disorders including Alzheimer's and Parkinson's. One study found that *Bacopa monnieri* may help to protect against oxidative stress and improve the growth and function of nerve cells in the brain.[2]

Other Potential Medicinal Uses

In addition to the above-mentioned benefits, *Bacopa monnieri* has been studied for its potential to treat a variety of other health conditions. For example, the herb has been shown to have potential as an antidepressant, a treatment for epilepsy, and a treatment for gastric ulcers. It may also have potential as a treatment for skin disorders such as eczema and psoriasis.

Overall, *Bacopa monnieri* is a promising herb with a variety of potential medicinal uses. While more research is need to fully understand its biological properties and potential therapeutic benefits, the herb has a long history of use in traditional medicinal system and is increasingly being studied by modern scientists.

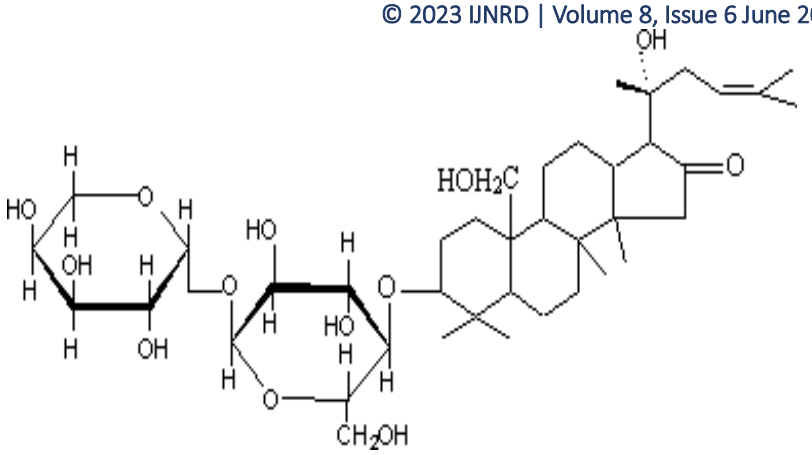
Classification -

- Kingdom - Plantae
- Phylum - Mangoliophyta
- Class - Mangolopsida
- Order - Lamiales
- Family - Scrophulariaceae
- Genus - *Bacopa*
- Species - *monnieri*

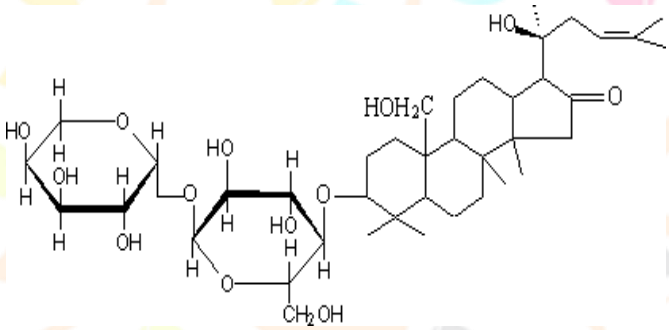
Active Constituents

The main chemical component identified as bacoside A, also known as 3-(L-arabinopyranosyl)-O-D-glucopyranoside-10,20-dihydroxy-16-keto-dammar-24-ene, is believed to be responsible for the herb *Bacopa monnieri's* memory-enhancing effects. Bacoside A and bacoside B typically co-occur; the latter differs mainly in optical gyration and is likely an artefact created during the separation of bacoside A. [10]

Several glycosides, flavonoids, phytochemicals similar brahamoside, brahminoside, brahmic acid, etc., as well as betulinic acid, wogonin, oroxindin, betulic acid, stigmastarol, beta-sitosterol, etc. Additional information about the chemical components was obtained through the isolation of D-mannitol and many salts of saponin, hersaponin, and potassium.



Bacosides A



Bacosides B

Mechanism of action

The majority of the research has been concentrated on the mechanism underlying these features because *Bacopa's* main therapeutic application is to improve cognitive function. *Bacopa's* capacity to improve nerve impulse transmission is due to the triterpenoid saponins and related bacosides.

The bacosides support in the repair of injured neurons by encouraging kinase activity, neuronal synthesis, synaptic activity restoration, and finally, nerve impulse transmission. Additionally, they encourage the synthesis of new proteins in the brain.

Studies on animals show that bacopa extracts change the expression of particular enzymes involved in the generation and scavenging of reactive oxygen species in the brain. Additionally, in vitro studies have demonstrated that *Bacopa* has a preventive effect against DNA deterioration in human fibroblasts and astrocytes. *Bacopa* extracts may have an anticancer effect, according to in vitro research, which may be because they reduce the rate of DNA replication in cancer cell lines. .

Glucosyltransferase

Glycosyltransferases (GTs) are enzymes that catalyse the transfer of sugar moieties from donor molecules, which are often nucleoside diphospho-sugars, to certain acceptor molecules, which can be a lipid, a protein, or a developing oligosaccharide.[3] This creates glycosidic linkages.Glycosyltransferases are the enzyme that catalyzes glycosidic bond formation using nucleotide diphosphate activated sugar from protein, lipids, nucleic acids to the acceptor substrates such as nucleic acids, lipids, saccharides and low molecular weights such as secondary metabolites[3]. These enzymes are present in various living organisms but are most important in plants, which convert glucose and water into disaccharide, polysaccharide, and oligosaccharide. In plants, glycosyltransferases catalyzed the biosynthesis of cell wall polysaccharide. Glycosyltransferase also catalyzes the transfer of sugar residues onto aglycons, which is more important for the synthesis of many high-value products. Glycosyltransferases that uses sugar moieties as a donor substrate are referred to as a Loloir enzyme, after the scientist Luis F. Leloir who identified the first nucleotide sugar. For this work, he was awarded the Nobel Prize in Chemistry in 1970. Numerous glycosyltransferase genes have been discovered in recent years, and many of these have undergone functional characterization. It is now known that adding a sugar moiety to the acceptors of low-molecular-weight plant compounds typically alters the acceptors' bioactivity, stability, solubility, subcellular localization, and capacity to bind to other molecules, potentially reducing the toxicity of both endogenous and exogenous toxic substances. In order to maintain cell homeostasis and control plant growth, development, and defence mechanisms in stressful conditions, glycosyltransferases may be crucial. Research on glycosyltransferases and the glycosylation of plant molecules has drawn interest from scientists because knowing the enzymes' catalytic mechanisms and physiological roles would be crucial for the in vitro design and synthesis of valuable glycosides. Up until now, studies on glycosyltransferases and glycosylation towards low-molecular-weight plant compounds have mostly concentrated on Arabidopsis and a few other plant species. Functional genomics methods, in particular the procedures of gene over-expression and gene knock-out (or knock-down), along with the availability of significant biochemical data and genomic data on plant GTs, have made it possible to examine the biological functions of GTs in plants. Recent findings from the functional characterization of plant GTs suggest that glycosyltransferases may be crucial for plant development, growth, and interaction with the environment.

Classification of glycosyltransferases

According to CAZy databases, glycosyltransferases are classified into 107 families.[7] According to the IUBMB guidelines, glycosyltransferases have discrete Enzyme Commission numbers. These are classified on the basis of different parameters on the basis of similarities in amino acids,, reaction mechanism, substrate specificity, 3D structures (GT-A, GT-B and GT-C folds) and type of reaction. The maximum number of UGT genes are present in GT-1 family. From the limited of sequences available and by using hydrophobic cluster analysis (HCA) and BLAST, the CAZy families were created.[4] To be categorized under the same family, an E-value should be under 0.001 throughout 100 amino acids is required. By the help of BLAST and HMMER based sequence similarity methods, the database was subsequently complimented. GT 1 and GT 31 are the common major GT families in *A thaliana*, *O*

sativa, Humans, *C. elegans*, *D. melanogaster*. Genes in the GT 2, GT 8, GT 47 are specifics to the plants, those genes in GT11, GT 14, GT 92 are specific to *C. elegans*, and those genes in GT 29 are Human-specific. These specificities can represent distinctive elements of each organization's metabolism for examples GT 2, GT8 and GT 47 families have involved those enzymes which are helpful in the biosynthesis of plants .

Role of Glycosyltransferases

Recent outcomes are observed that efficient characterization of plant Glycosyltransferases may assume a significant job in plant development, growth, and interaction with nature.

Detoxification

Glycosyltransferases also play a crucial part in detoxification. Some fungal pathogen detoxifies the glycosidic molecule. This is performed by breaking down the glycosidic linkages. However, in the conflict among the pathogens and plants, the glycosidic bonds are formed by the plants to detoxify the toxicity of the pathogens. *Fungus Fusarium* is a fungus generally found infecting maize, wheat, and barley, etc. It produces trichothecene deoxynivalenol which also got detoxified which otherwise act as a potent virulence factor in fungal pathogenesis. By doing in-vitro experiments, it was observed that putative glycosyltransferases of *Arabidopsis* (UGT73C5), could catalyze the conversion of DON to non-toxic DON-3-O-glucoside. Overexpressing UGT73C5 in Arabidopsis could increase the resistance of transgenic to DON, and glycosylated DON also loses toxicity .

Defence reaction

There are several instances that involve the function of secondary metabolite glycosylation in responding to biotic stress in plant defense. It was observed that by decreasing the expression of TOGTs (Tobacco glycosyltransferases that have highest enzyme activities towards hydroxycinnamic acids, hydroxycoumarin, and scopoletin) in transgenic tobacco lead to the weakening in the resistance of Tobacco Mosaic Virus (TMV) Simultaneously, it reduced the level of scopoletin glucoside. The overexpression of TOGT 1 in tobacco-caused increased resistance towards Tomato Virus Y [6]

Involved in Secondary metabolites biosynthesis

Monoterpenoids, flavonols and hydroxybenzoic acids, are secondary metabolites usually accumulate in plants as aglycones and glycosides. From *Arabidopsis,* three glycosyltransferases (UGT75C1, UGT78D2, and UGT79B1) were isolated by Jones et al. It was a component in flavonol glycosides' biosynthesis. Glycosylation is the last step in the biosynthesis of the flavonol.

Stabilization of Secondary Metabolites

Stabilization of phytomolecules is an important part of glycosyltransferases. For examples, Anthocyanin is flavonoids pigments that accumulate in the vacuole represent the secondary metabolism; this study has been taken along with stabilization versus glycoside formation. In the cytosol, along with the glycosylation, the acylation of sugars takes place, and after this, the transportable conjugated anthocyanins were made to get together in the vacuole. The glycosylation plays an important part in structure maintenance, integrity, and stability of flavylium cation but not takes part in color formation of the anthocyanin structures. The mutational changes in the grapevine resulted in the reduction of anthocyanidin glucosyltransferases resulting in the anthocyanidin-less berries[8]. To inhibit the conversion of anthocyanidin into non-colored form, glycosylation at C-3, C-5, and C-7 were takes place to prevent its breakdown and stability of molecules.

Crop Improvements

Application of genetic manipulation of crops in biotechnology is important for a better quality of crops. There are many roles of glycosyltransferases like from defense mechanism to detoxification, hormone homeostasis, biosynthesis of secondary metabolism, and stability of molecules give an important application in transgenic with improved crops[6]. For examples, glycosyltransferases taking part in hormone homeostases such as cytokinin, auxin, and brassinosteroids, by increasing or decreasing the level of hormones, it affects the crops with desired phenotypes because these hormones impacts on the growth and developments of plants. Other examples of crop improvements are insertion of those glycosyltransferases participates in detoxification to pesticides and xenobiotics for the good quality and quantity of food, safety, and by doing this the developed transgenic plant have the capability to resist against biotic and abiotic stress and increased level of glycosides in foods with cancer prevention as well as antioxidant characteristics.

Conclusion:

In conclusion, *Bacopa monnieri*, also known as Brahmi, is a medicinal plant that has been used for centuries in traditional medicine systems. It has a rich history of use in Ayurveda and other traditional systems, where it is believed to enhance cognitive function, improve memory, reduce stress and anxiety, and have antioxidant properties. Modern scientific research has provided evidence supporting some of these traditional uses and has also uncovered new potential medicinal benefits of *Bacopa monnieri*.Studies have shown that *Bacopa monnieri* can enhance cognitive performance, including memory, attention, and learning. It may achieve this by increasing the production of neurotransmitters such as acetylcholine, which are essential for cognitive function. Additionally, *Bacopa monnieri* has been found to have anxiolytic and stress-reducing effects, making it a potential natural remedy for anxiety disorders. Its anti-inflammatory and antioxidant properties make it a promising candidate for treating various medical conditions associated with inflammation and oxidative stress.Moreover, *Bacopa monnieri* exhibits neuroprotective properties, suggesting its potential in preventing age-related cognitive decline and neurodegenerative disorders like Alzheimer's

and Parkinson's diseases. It has shown promising results in protecting against oxidative stress and promoting the growth and function of nerve cells in the brain.Glycosyltransferases, a class of enzymes involved in glycosylation reactions, may play a significant role in preserving cell homeostasis and regulating plant development and defense mechanisms under stressed conditions. The glycosylation process results in the formation of natural glucosides and may be the final stage in the production of secondary metabolites. Understanding the catalytic mechanisms and physiological roles of glycosyltransferases is essential for the design and synthesis of valuable glycosides.

Future Perspective-

In future research, further exploration of *Bacopa monnieri's* medicinal properties and mechanisms of action, particularly related to glycosylation and the role of glycosyltransferases, would be valuable. Investigating the potential of *Bacopa monnieri* in the treatment of various health conditions, such as depression, epilepsy, and skin disorders, could provide insights into its broader therapeutic applications. Additionally, exploring the industrial and commercial potential of *Bacopa monnieri*, including its use as a memory-enhancing drug and its incorporation into functional foods and nutraceuticals, would be of interest.Overall, *Bacopa monnieri* shows great promise as a natural remedy with diverse medicinal properties. Continued research and development of this plant, along with a deeper understanding of glycosylation processes and the role of glycosyltransferases, could lead to the discovery of new therapeutic applications and the development of innovative products for healthcare and well-being.

References -

1. Abhyankar GA and Chinchanikar GS (1996). Response of Withania somnifera Dunal leaf explants in vitro. *Phytomorphology* 46(3): 249-252.
2. Aguiar S, Borowski T (2013). Neuropharmacological review of the nootropic herb *Bacopa monnieri*. *RejuvenationRes*. 16: 313–326.
3. Bowles D, Isayenkova J, Lim E K, Poppenberger B (2005). Glycosyltransferases: managers of small molecules. *Curr Opin Plant Bio.* 8: 254–263.
4. Campbell JA, Davies GJ, Bulone V, Henrissat B (1997). A classification of nucleotide-diphospho-sugar glycosyltransferases based on amino acid sequence similarities. Biochem. J. 326: 929-939.
5. Campbell JA, Davies GJ, Bulone V, Henrissat B (1997). A classification of nucleotide diphospho-sugar glycosyltransferases based on amino acid sequence similarities. *Biochem. J.* 326: 929–939.
6. Chong J, Baltz R, Schmitt C, Beffa R, Fritig B, Saindrenan P (2002). Down-regulation of a pathogen-responsive tobacco UDP-Glc: phenylpropanoid glucosyltransferase reduces scopoletin glucoside accumulation, enhances oxidative stress, and weakens virus resistance. *Plant Cell*. 14: 1093–1107.
7. Coutinho PM, Deleury E, Davies GJ and Henrissat B (2003). An evolving hierarchical family classification for glycosyltransferases. *J. Mol. Biol.* 328: 307–317.

8. Creelman R A and Mullet J E (1997). Biosynthesis and action of jasmonates in plants. Plant Mol Biol, 48: 355–381.

9. Deb DD, Kapoor P, Dighe RP, Padmaja R, Anand MS, D'Souza P, Deepak M, Mural B and Agrawal A (2008). *In vitro* safety evaluation and anticlastogenic effects of BacoMindTM on human lymphocytes. *Biomed Environ Sci* 21(1): 7–23.

10. Deepak M, Sangli GK, Arun PC and Amit A (2005). Quantitative determination of the major saponin mixture bacoside A in *Bacopa monnieri* by HPLC. *Phytochemical Analysis: An International Journal of Plant Chemical and Biochemical Techniques*. *16*(1): 24-29.