Recent Progress on Chemical Composition and Bioactivities of Bacopa monnieri (Linn.) a Plant of Ayurveda

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ABSTRACT

Bacopa monnieri (Linn.) is a highly regarded medicinal plant in Indian traditional Ayurvedic medicine for centuries owing to its broad spectrum bioactivities. The biological effects of B. monnieri are documented in traditional as well as scientific literature. The plant possess many important bioactivities like memory enhancing, anti-oxidant, anti-inflammatory, analgesic, antipyretic, hepatoprotective, sedative, anti-epileptic and still many more are constantly being discovered. An ample amount of research on B. monnieri and its major constituents has unraveled its tremendous bioactive potential in the treatment of many serious disorders viz. Alzheimer’s disease, cognitive functions, memory impairment, hepatic carcinoma and cigarette smoking-associated diseases. Since 2005, when the last review on B. monnieri was written, many more new bioactivities have been discovered, although they have not been compiled in one publication. In the present article we describe many new useful bioactivities of B. monnieri and its active chemical constituent bacoside and new chemical constituents that have been isolated and characterized.

Keywords: anti-Alzheimer’s, antiimmunotoxic, Bacopa monnieri, bacoside, neuroprotective, saponin, Scrophulariaceae

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INTRODUCTION

Bacopa monnieri (Linn.) belongs to the Scrophulariaceae family and has been a reputed medicinal plant in Indian traditional Ayurvedic system for 3000 years. It is a perennial creeping plant distributed in Fujian, Taiwan, and in Guangdong, Yunnan, and Sichuan Provinces in China. The plant is found throughout the Indo-Pakistan subcontinent in wet, damp and marshy areas and is locally known as Brahmi (Satyavati et al. 1976). The plant improves the brain health hence it has been given the name Brahmi which is derived from the word Brama (Russo and Borrelli 2005).

The tremendous medicinal and pharmacological significance of B. monnieri and chemical constituents therein has always attracted the attention of researchers. Many previously published reports have documented the use of B. monnieri for insanity, nervous breakdown, dermatitis and in memory enhancement (Chopra et al. 1998) antiulcerogenic, adaptogenic activities and hepatoprotective effect against morphine induced liver toxicity in rats (Russo and Borrelli 2005; Sumathi and Niangbri 2008). It helps in prevention of neurological diseases (Vohora et al. 2000) and possessed anti-inflammatory, analgesic, antipyretic, sedative (Kishore and Singh 2005), free radical scavenging and lipid peroxidative activities (Anbarasi et al. 2005a, 2005b). The plant also possesses anti-addictive and mast cell stabilizing properties (Samiulla et al. 2001).

In recent years, many newer bioactivities of B. monnieri plant and pure chemical constituents have been rapidly deciphered; as a result, the pharmacological and medicinal value of the plant has been tremendously increased. Potential effects of B. monnieri on nitrobenzene induced liver damage in rats have been reported (Menon et al. 2010). Several recent studies have indicated beneficial effects of B. monnieri on cognitive functions, against the β-amyloid protein and glutamate-induced neurotoxicity in primary cortical cultured neurons in Alzheimer’s disease (AD) patients (Dhansekaran et al. 2007; Limpeanchob et al. 2008; Uabun-
At least 70 chemical constituents have been isolated from the whole plant of *B. monnieri* (Zhou et al. 2009b). The major chemical constituents identified are dammarane-type of triterpenoid saponins with jujubogenin or pseudo-jujubogenin moieties as aglycone units (Chillara et al. 2005). The biological activities of *B. monnieri* have been mainly attributed to these saponins especially, bacopside-A and bacoside-B (Deepak and Amit 2005). Compounds like polyphenols and sulphhydril having endogenous antioxidant activity have been responsible for anti-AD property of *B. monnieri*. Bioactive potential of *B. monnieri* accessions to biosynthesise bacoside-A has been studied using 14C-labelled CO2 (Ganjewala et al. 2009b). Significant ontogenic and seasonal variation in accumulation pattern of bacoside-A in five different accessions of *B. monnieri* have also been reported (Ganjewala et al. 2009b). Dammarane triterpenoid saponins such as bacopasides E and VII possess potential antioxidant and cytotoxic activities (Peng et al. 2010).

**NEW CHEMICAL CONSTITUENTS FROM BACOPA MONNIERA**

Zhou et al. (2009b) isolated a new triterpenoid saponin, bacopside IX (3-O-[β-D-glucopyranosyl(1→4)→[α-L-arabinofuranosyl-(1→2)]-β-D-glucopyranosyl]-20-O-Mercapto-β-D-glucopyranosyl) from the whole plant of *B. monnieri* (L.) Earlier, Chillara et al. (2005) have isolated two new triterpenoid glycosides 3-O-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl) jujubogenin and 3-O-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl) pseudofujiugenin along with 10 known saponins from *B. monnieri*. Two new dammarane-type triterpenoid saponins, bacopasides-XI (3-O-[α-L-arabinofuranosyl(1→3)]-6-O-sulfonyl-β-D-glucopyranosyl) and XII (3-O-[α-L-arabinofuranosyl(1→3)]-6-O-sulfonyl-β-D-glucopyranosyl) have also been isolated from *B. monnieri* (Zhou et al. 2009b).
B. monnieri is an excellent medicinal plant offering many promising pharmacological activities important for the treatment of many complex diseases/disorders. The newer most promising bioactivities are antiinflammatory, protective/antioxidant, hepatoprotective, cardioprotective, non-steroidal anti-inflammatory, anti-Alzheimer’s, nortropic, anti-aging, memory enhancement, anti-arithmetic and anti-tumor, cytotoxic and chemopreventive (Table 1). In the following sections these bioactivities, with brief information of their mechanism have been discussed.

Protective effects/antioxidant activities

Nearly 35-40% of the world’s population used to smoke. The number of people exposed to environmental tobacco smoke is increasing rapidly. Free radicals and oxidative damage play crucial roles in the pathogenesis of smoking-related diseases. Cigarette smoking causes free radical-mediated lipid peroxidation (LPO) leading to increased membrane permeability and cellular damage in the heart and brain (Anbarasi et al. 2005a, 2005b). Bacoside-A, a dammarane type of triterpenoid isolated from B. monnieri has been known for its strong antioxidant potential is useful in protection against cigarette smoking-induced toxicity as well as in diabetic complications such as neuropathy, nephropathy and cardiopathy occurred due to oxidative damage (Anbarasi et al. 2005a, 2005b; Kapoor et al. 2009). Protective effect of bacoside-A against smoking-induced toxicity in rat brain has been reported (Anbarasi et al. 2005a, 2005b). For the assessment of antioxidant potential of bacoside-A against cigarette smoking-induced toxicity, activities of enzymes such as lactate dehydrogenase (LDH), creatine kinase (CK) with their isoenzymes have been monitored in rats (Anbarasi et al. 2005a, 2005b). Bacoside-A being a powerful free radical scavenger and anti-lipid peroxidative agent prevented the release of LDH (Anbarasi et al. 2005a). A similar study by Anbarasi et al. (2005b) reported protective effects of bacoside-A; however, in this study CK and its isoenzymes were used as sensitive markers for the potent amount of cerebral damage occurred due to oxidative damage. Results of the study revealed that cigarette induced smoking in albino male causes a significant increase in activities of the serum CK and isoenzymes, but decreases in the heart and brain. Exposure to cigarette smoking leads to an increase in LPO, membrane permeability and cellular damage in the heart and brain causing release of CK into the circulation (Anbarasi et al. 2005b). Bacoside-A prevents the leakage of CK from the respective tissues as it has protective effects on the structural and functional integrity of the membrane.

Two more studies have reported similar protective roles of bacoside-A against oxidative stress in the brain of rats exposed to cigarette smoke (Anbarasi et al. 2006a, 2006b). The brain is highly susceptible to free radical attack; however, it produces more free radicals per gram of tissue than does any other organs but lack sufficient enough amounts of protective antioxidants (Arivazhagan et al. 2002). Application of bacoside-A as being a strong antioxidant could be a very effective strategy for brain to overcome effects of oxidative damages (Anbarasi et al. 2006a). A study by Anbarasi et al. (2006a) confirmed the neuroprotective effects of bacoside-A against chronic cigarette smoking induced oxidative damage in rat brain. Antioxidant status of rat brain after treatment with bacoside-A have been evaluated by measuring the changes in the level of reduced glutathione, vitamin C, E, and A, superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase as well as copper, iron, zinc and selenium in brain and serum ceruloplasmin activity (Anbarasi et al. 2006a). A substantial increase in the antioxidant status while maintaining the levels of trace elements has been observed in rats following bacoside-A treatment (Anbarasi et al. 2006a). These studies have clearly suggested that cigarette smoking associated diseases might be prevented by application of bacoside-A like bacosate-A. A study has described that cigarette smoking exceptionally increases oxidative damages and induces expression of heat shock protein-70 (hsp-70) and apoptosis (Anbarasi et al. 2006b). Expression of hsp-70 and apoptosis becomes pronounced during cigarette smoking toxicity and pathogenesis. Since the bacosate-A hinders both expression of hsp-70 and apoptosis it may provide protection to the brain of smoking-induced rats from the toxic effects of cigarette smoking (Anbarasi et al. 2006b).

Concurrently, the bacosate-A has shown similar protective roles in diabetic complications such as neuropathy, nephropathy and cardiopath which occurs as result of oxidative stress damages (Kapoor et al. 2009). A study performed with streptozotocin induced diabetic rats has revealed the protective effects of B. monnieri extract on tissue antioxidant status and LPO (Kapoor et al. 2009). Extract of B. monnieri most likely shield tissues from the attack of reactive oxygen species (ROS) in diabetic rats via modulation of antioxidant defense system (Kapoor et al. 2009). Protective effect of B. monnieri extract in this study has been substantiated by measuring activities of enzymes of antioxidant status such as, superoxide dismutase (SOD) cataease (CAT), glutathione peroxidase (Gpx) and glutathione reductase (GSH) in diabetic rats after administration of bacosate extract. Vijayan and Helen (2007) studied the geneprotective effect of B. monnieri aqueous extract in nicotine-induced toxicity Swiss mice (Vijayan and Helen 2007). Nicotine an active component of cigarettes smoke exert devastating effects by generation of free radicals on important biomolecules of the cell leading to genomic instability. For the investigation of effects of B. monnieri aqueous extract on genomic stability and LPO, micronucleus assay was performed and the levels of malondialdehyde (MDA) measured (Vijayan and Helen 2007).

Aluminium and its salts have been reported to cause oxidative damages to bio-molecules like lipids, proteins and nucleic acids which lead to neurotoxicity. Extracts of B. monnieri have shown protective effects against aluminium-induced oxidative stress in the hippocampus and cerebral cortex in male Wistar rats (Jyoti and Sharma 2006). B. monnieri has demonstrated beneficial effects against neurotoxicity in brain occurred due to oxidative stress damages in male Wister rats (Jyoti et al. 2007).

For the first time potential of B. monnieri to modulate endogenous markers of oxidative stress in brain tissue of prepubertal (PP) mice has been evaluated recently by Shnimol and Muraidhara (2011). Their study suggested that dietary intake of B. monnieri leaf powder confers neuroprotective advantage and might be used as a prophylactic/therapeutic agent for neurodegenerative disorders involving oxidative stress (Shnimol and Muralidhara 2011). Dietary intake of B. monnieri significantly diminished basal oxidative markers (MDA levels, ROS generation, hydroperoxide levels and protein carbonyls) with corresponding increase in the levels of reduced glutathione, thiol and activity of antioxidant enzymes (catalase, peroxidase, superoxide dismutase) in both cytoplasm and mitochondria in various brain regions of prepubertal (PP) mice. Also, B. monnieri leaf powder has a property to modulate cholinergic function by significantly reducing the activity of acetyl cholinesterase in all regions of the brain. Examination of cortical/cerebellar synaptosomes of normal and B. monnieri fed mice exposed to 3-nitropropionic acid (3-NPA) provided more evidence that dietary intake of B. monnieri leaf powder confers the prepubetal brain with
additional capacity to cope with neurotoxic pro-oxidants. The results showed that control mice exhibited a concentra-
tion related LPO and ROS generation while synaptosomes
obtained from B. monnieri fed mice showed only a marginal
induction at the highest concentration clearly suggesting
their increased resistance to 3-NPA-induced oxidative stress
(Shinomol and Muralidharan 2011).

Nootropic, anti-aging and memory-enhancing activities

B. monnieri has been used in India for centuries as an anti-
aging and memory-enhancing ethno-botanical therapy (Hol-
comb et al. 2006). The standardized extract of B. monnieri
have been reported to improve behavioural learning infor-
mation processing in subjects with age-associated memory
impairment without any evidence of dementia or psychiatric
disorder (Raghav et al. 2006). Three new saponins from B.
monnieri namely, bacopaside 3, bacopaside I and bacopa-
saponin C are reported to have nootropic activity and im-
proves scopolamine-induced memory impairment in mice
(Zhou et al. 2009b). B. monnieri leaf extract rich in the
bacoside content has therapeutic potential of improving the
memory functions in hypobaric conditions simulating an
altitude of 25,000 ft for different durations in male Sprague-
Dawley rats (Hota et al. 2009). Beneficial effect of admin-
istration of bacopaside on apoptosis, cytochrome c oxidase
activity, ATP levels, and oxidative stress markers and on plasma
corticosterone levels has been reported. Bacosides are ex-
cellent therapeutic agent in ameliorating hypobaric hypoxia
induced cognitive dysfunctions and other related neurolo-
gical disorders (Hota et al. 2009). The mechanism of the
bacopaside action was elucidated by studying expression of
NR1 subunit of N-methyl-d-aspartate receptors, neuronal
cell adhesion molecules and cAMP response element-bind-
ing protein phosphorylation. A recent study revealed that B.
monnieri leaf ethanol extract is useful for memory enhance-
ment through up-regulation of expression of tryptophan
hydroxylase (TPH2) and serotonin transporter system
(Charles et al. 2011). Techniques like enzyme linked im-
unosorbent assay and semi-quantitative polymerase chain
reaction has been used to evaluate the effects of B. monnieri
leaf ethanol extract on neurotransmitter system in rats.

Although, B. monnieri has been known for centuries in
Ayurveda for cognitive improving effects several recently
published reports have consolidated these findings. A special extract (Stough et al. 2008) and lipid-based extract of
B. monnieri (Lohidasan et al. 2009) have been reported to
demonstrate nootropic effects. Neuropsychological ef-
fects of B. monnieri have been tested using the Cognitive
Drug Research cognitive assessment system. B. monnieri
special extract significantly improved performance of the
‘Working Memory’ factor, more specifically spatial work-
ing memory accuracy (Stough et al. 2008). B. monnieri
plants have the property of prevention of formation of MDA
and lipofuscin pigments in prostate gland of D-galactose in-
duced aging mice, Mus musculus (Kalamade et al. 2008).

Anti-amnesic activities

Several research groups working on B. monnieri have
investigated anti-amnesia properties for the development of
new potential drugs for amnesia. Amnesia is a condition
results from ageing, chronic drug abuse or head injury for
which currently limited therapeutics are available. However,
recent studies have revealed potential anti-amnesic proper-
ties of B. monnieri that could be useful in alleviating amne-
sia (Anand et al. 2010). Studies have revealed that adminis-
tration of B. monnieri extract may reverse both dizepamz
and scopolamine induced amnesia in mice (Saraf et al. 2008,
2010). Most likely B. monnieri antagonizes MK801, an
NMDA receptor antagonist and N(o)-nitro-L-arginine (L-
NNA), a nitric oxide synthase inhibitor. The antiamnesic
effect B. monniera on L-NNA induced amnesia are possibly
mediated by nitric oxide (NO) pathway with involvement of
calmodulin (CaM), which is required for long-term poten-
tiation (LTP) sustenance (Anand et al. 2010). Scopolamine
has been known as an anticholinergic drug produce amnesia
by interference of LTP. It is used for discerning the efficacy of
various anti-amnesic drugs (Saraf et al. 2008). B. monnieri
has been found to improve CaM significantly and it par-
tially attenuates activity of protein kinase C and pCREB,
these properties have been postulated for anti-amnesic effects
in scopolamine induced amnesia in rats. The study has clearly
indicated major role of CaM in anti-amnesic effects of
B. monnieri. Kishore and Singh (2005) have reported
anti-amnesic effects of alcoholic extract of B. monnieri and
the bacosides on experimental amnesia in mice induced by
scopolamine, sodium nitrite, and BNS5201. Properties of
bacosides to improve acetylcholine level and hypoxic
conditions are the most likely factors responsible for anti-
amnesic effects of B. monnieri (Kishore and Singh 2005).
Bacosides are also found to increase synthesis of platelet
activating factor by enhancing cerebral glutamate level
(Kishore and Singh 2005).

Anti-inflammatory activities

For very long time B. monnieri has been described as a the-
rapeutically useful herb for the treatment of inflammation.
Channa et al. (2006) have reported potential anti-inflam-
matory properties of B. monnieri. The ethanol extract of B.
monnieri has demonstrated strong anti-inflammatory activi-
ty against carrageenan-induced paw edema in mice and rats.
The anti-inflammatory activity of the ethanol extracts
however has been observed only in rats those treated with
chemical mediator prostaglandin E2 but not against car-
rageenan, in histamine, serotonin, bradykinin and arachi-
donic acid-induced edema in rats (Channa et al. 2006).
Most defined work on anti-inflammatory potential of B.
monnieri and its mechanism of action have been carried out
Efficacy of B. monnieri methanol extracts in modulating
key mediators of inflammation using carrageenan-induced
rat paw edema, rat mononuclear cells and human whole
blood assay have been evaluated (Viji and Helen 2008).
Methanol extract of B. monniera demonstrated a strong
anti-inflammatory activity which has been attributed to its
tendency to inhibit activities of cyclooxygenase-2 and lipo-
oxidase and down regulation of tumor necrosis factor
(TNF)-α and interleukin-6 (IL-6) (Viji and Helen 2008).
A similar study has reported the anti-inflammatory activity of
B. monnieri methanol extract rich in triterpenoid and baco-
sides content (Viji and Helen 2010). The inhibitory proper-
ties of B. monniera methanol extract on the production of
pro-inflammatory cytokines such as, TNF-α and IL-6 is
assumed to be responsible for anti-inflammatory activity
(Viji and Helen 2010). Both the triterpenoid and bacosides
present in methanol extract of B. monnieri demonstrated
anti-oxidematogetic effect in carrageenan-induced hind paw
edema mice; however, a methanol extract containing triter-
penoid only showed anti-inflammatory activity in the arthritis
model (Viji and Helen 2010). Betulinic acid a pentacyclic
triterpenoid present in the B. monniera also possesses anti-
flammatory activity (Viji et al. 2010b). Betulinic acid
suppresses the production of IL-6 as a result of lipopolysac-
charide induction in blood mononuclear cells both in vivo
and in vitro. It inhibits production of IL-6 by preventing
65 KD protein nuclear factor κB (p65 NF-κB) nuclear trans-
location. Other factors p38 and extracellular-signal-regu-
lated kinases and mitogen-activated protein kinases are also
involved in prevention of p65 NF-κB nuclear translocation
(Viji et al 2010a).

Anti-epileptic activities

Epilepsy is a neuronal disorder characterized by learning,
cognitive and memory impairments (Mathew et al. 2010a).
B. monnieri has been used for long time as nerve tonic for
improving the mental performance. The plant molecules
from *B. monnieri* have beneficial properties of suppressing the seizure/convulsion in worms (*Caenorhabditis elegans*) (Pandey et al. 2010). The 1-mm long *Caenorhabditis elegans* is one of the prime research tools to study different human neurodegenerative diseases. The occurrence of seizures causing the impairment of peripheral nervous system in pilocarpine-induced epileptic rats could be well prevented by application of *B. monnieri* and the bacoside-A (Mathew et al. 2010d). Application of *B. monnieri* and the bacoside-A in epileptic rats was found to increase acetylcholine esterase and malate dehydrogenase activity in the muscle and decrease in the heart. The bacoside-A treatment also significantly influence insulin and T3 content in the serum of the epileptic rats (Mathew et al. 2010b). Recent studies have indicated the roles of gamma-amino butyric acid-A (GABA-A) receptors in epilepsy associated motor learning deficits (Mathew et al. 2010c, 2010d). The group of Mathew and coworkers has carried out the most defined work on GABA receptors and their association with learning deficit in epileptic rats. A study aimed to evaluate potential of *B. monnieri* and the bacoside-A on spatial recognition memory deficit and alterations of GABA receptor in the striatum of epileptic rats has revealed that application of *B. monnieri* and bacoside-A can reverse the changes in memory deficit and alterations of GABA-A receptor (Mathew et al. 2010c). Another study by this group has found the similar effects of *B. monnieri* and bacoside-A, on motor deficit and alterations of GABA-A receptor functional regulation in the cerebellum of epileptic rats (Mathew et al. 2010d). The study suggested that the occurrences of repetitive seizures induce GABAergic activity, motor learning, and memory deficit in epileptic rats. Application of *B. monnieri* and bacoside-A most likely prevents the occurrence of seizures and may reduce the impairment of GABAergic activity, motor learning, and memory deficit in epileptic rats. In these studies, total GABA and GABA-A receptor numbers in the control and epileptic rats have been evaluated using [(3)H]GABA and [(3)H]bicuculline binding. Also studied the GABA(Au1), GABA(Au5), GABA(Au3) and GABA(AD) gene expressions levels. Please refer an article by Mathew et al. (2010a) for details on beneficial effect of *B. monnieri* on epilepsy-associated behavioral deficits.

Anti-Alzheimer’s activities

Several recently published reports have recognized the anti-AD potential of *B. monnieri*. AD is one of the most common neurodegenerative disorders affects many elderly people (Limpeanchob et al. 2010). Presently, there is no drug or therapy is available as definite solution for neurodegenerative disorders affects many elderly people (Limpeanchob et al. 2010). Still, the mechanism of action of these compounds and the bacoside-A can reverse the changes in memory deficit and alterations of GABA-A receptor functional regulation in the cerebellum of epileptic rats (Mathew et al. 2010d). The study suggested that the occurrences of repetitive seizures induce GABAergic activity, motor learning, and memory deficit in epileptic rats. Application of *B. monnieri* and bacoside-A most likely prevents the occurrence of seizures and may reduce the impairment of GABAergic activity, motor learning, and memory deficit in epileptic rats. In these studies, total GABA and GABA-A receptor numbers in the control and epileptic rats have been evaluated using [(3)H]GABA and [(3)H]bicuculline binding. Also studied the GABA(Au1), GABA(Au5), GABA(Au3) and GABA(AD) gene expressions levels. Please refer an article by Mathew et al. (2010a) for details on beneficial effect of *B. monnieri* on epilepsy-associated behavioral deficits.

Anti-arthritic activities

Recent study using a type II collagen-induced arthritis rat model has revealed *B. monnieri* potential to treat rheumatoid arthritis (Viji et al. 2010b). Antiinflammatory potential of plant extract has been evaluated after inducing arthritis in male Wistar rats by immunization with bovine type II collagen in complete Freund’s adjuvant. *B. monnieri* extract have shown beneficial effects on several selected parameters viz. paw swelling, arthritic index, cyclooxygenase, lipooxygenase, myeloperoxidase and serum anti-collagen immunoglobulins (IgG and IgM) levels in Wistar rats (Viji et al. 2010b). The ability of *B. monnieri* in alleviating lysosomal instability in adjuvant-induced arthritis in rats has been reported (Vijayan et al. 2010). It has been suggested that *B. monnieri* extract may stabilize lysosomal membranes and decrease the spread of inflammation.

Anti-tumor/cytotoxic/chemopreventive activities

Anti-tumor activity is one of the most important activities of *B. monnieri* plant that has been recognized recently (Rohini and Devi 2008; Peng et al. 2010). The ethanol extract of *B. monnieri* can induce cell death by apoptosis in mouse S-180 cells (Rohini and Devi 2008). Peng et al. (2010) reported anti-tumor activities of *B. monnieri* extract and four different fractions prepared in petroleum ether, chloroform, ethyl acetate and butanol. Dammarane triterpene saponins viz., bacopasides E and VII present in the plant extract have potential anti-tumor and cytotoxic effects against human tumor cell lines (MDA-MB-231, SHG-44, HCT-8, A-549 and PC-3M). Anti-tumor effects were assessed by performing a 3-[4,5-dimethylthiazole-2-yl]-2,5-diphenyltetrazolium bromide assay (MTT) and in mouse implanted with sarcoma S180 in vivo (Peng et al. 2010). Still, the mechanism of action of these bacopasides remains to be elucidated. Previously, Pawar et al. (2007) isolated two new dammarane glycosides, the 20-deoxy derivatives of jujubogenin and pseudojujubogenin along with 8 new compounds and tested them for cytotoxic, antiinflammatory, antimicrobial, antioxidant, and anti-inflamatory activities. Not all, but some of these compounds demonstrated mild to moderate cytotoxic activity against...
non-cancerous kidney cell lines. Bacoside-A has been quite effective in preventing DEN-induced hepatocellular carcinoma by quenching LPO, enhancing antioxidant status, and protecting endogenous enzymatic and non-enzymatic antioxidant activity (Janani et al. 2010). Thus, the chemopreventive properties of the bacoside-A would be an effective alternative approach to control hepatocarcinogenesis.

**Hepatoprotective and cardio-protective activities**

Several reports have described the hepatoprotective properties of B. monnieri and its major constituent bacoside-A against liver and kidney injury in rats induced by selected compounds. Bacoside-A has been found to be a highly effective hepatoprotective agent against liver injury induced using D-GalN in rats (Sumathi and Nagbri 2008). With the application of bacoside-A in D-GalN induced rats, a sharp decrease was observed in the activities of enzymes, alanine transaminase, aspartate transaminase, alkaline phosphatase, g-glutamyl transferase, LDH and 50nucleotidase. Bacoside-A, however, helped to restore normal levels of vitamins C and E in the liver and plasma of D-GalN-induced rats (Sumathi and Nagbri 2008). Very similar hepatoprotective effects of B. monnieri leaf extract against morphine-induced liver and kidney toxicity in rats have also been reported (Sumathi and Devraj 2009). To assess the hepatoprotective effects, these authors studied the histopathological changes of liver and kidney as well as the activities of several relevant enzymes after administration of bacoside-A in morphine-induced rats. Pretreatment of bacoside-A prevents an elevation of LPO and activity of serum marker enzymes and maintains the antioxidant status during DEN-induced hepatotoxicity in the rats (Janani et al. 2009). The notorious carcinogenic DEN is reported to induce oxidative stress and cellular injury causing generation of ROS. In addition to its hepatoprotective properties, B. monnieri has also demonstrated cardioprotective effects in rat hearts following ischaemia-reperfusion (I-R) injury perfused in a Langendorff model (Mohanty et al. 2010). Cardioprotective effects of B. monnieri have been validated after measurement of activity of myocardial creatine phosphokinase and histopathological examination in the experimental model of ischaemia-reperfusion injury (Mohanty et al. 2010). These studies provide a basis for the alleged therapeutic use of B. monnieri and bacoside-A in liver and kidney injury as well as ischaemic heart diseases.

**Other useful bioactivities**

Besides the above important bioactivities, some other useful bioactivities of B. monnieri have also been investigated. Bacosine, a triterpene isolated from the ethyl acetate fraction of the ethanolic extract of B. monnieri, demonstrated antihyperglycemic activity in diabetic rats (Ghosh et al. 2011). Bacosine might have insulin-like activity and its antihyperglycemic effect might be due to an increase in peripheral glucose consumption as well as protection against oxidative damage in alloxanized diabetes (Ghosh et al. 2011). Sharath et al. (2010) described the wound-healing properties of the methanolic extract of B. monnieri and bacoside-A in excision, incision and dead space wounds on Swiss albino rats. The wound-healing activity of bacoside-A has been more effective in various wound models compared to the standard skin ointment Nitrofurazone. The effect of B. monnieri in the acquisition and expression of morphine tolerance in mice has been reported (Raut et al. 2010). Acute and chronic administration of 5, 10 and 15 mg/kg n-butanolic extract of B. monnieri resulted in a significant decrease both in expression and development of tolerance to morphine analgesia in mice. Also, B. monnieri enhanced the antioxidantic effect of morphine in intolerant animals.

**CONCLUSION**

Pharmaceutical and medicinal significance of Bacopa monnieri (Brahmi) is rapidly increasing. In this article we have discussed many newer useful bioactivities of B. monnieri and its major chemical constituents. The plant of B. monnieri has been in the center of researches since very long time owing to its tremendous pharmaco-active potential. Since ancient times B. monnieri has been an integral part of Indian and many other traditional medicinal systems used as nerve tonic, memory-enhancing, anti-inflammatory, analgesic, antipyretic, sedative, antioxidant and antitumor agents. In the past few years researches conducted on B. monnieri and its major constituents have elucidated many important bioactivities like antiinflammatory, antinflammatory, neuroprotective/ antioxidant, hepatoprotective, anti-epileptic, cardio protective, nootropic, anti-aging, memory enhancing, anti-arthritis and anti-tumor/cytotoxic/chemo-preventive activities. These new developments in pharmacological and medicinal research has evoked considerable interest in B. monnieri for its future development as potential drugs for AD and amnesia, respectively for which currently limited or no treatment is available. Concomitantly, significant progress has been made towards elucidation of the mechanism of action of B. monnieri extracts and its active ingredients. Perhaps more efforts are still needed to be devoted for deeper understanding of mechanism of action in case of Anti-Alzheimer, anti-tumor and chemopreventive properties of this plant. It is important to mention that until now most of the studies were aimed to investigate bioactivities of either B. monnieri leaf/whole plant extract or active constituent bacosides; however, no study were undertaken to evaluate the efficacy of B. monnieri if given together with other plants. Therefore, it is important to initiate studies to investigate if B. monnieri extract and its active constituents chronically exert more potent effects in combination with extracts of plants with similar medicinal value in the experimental models. Surprisingly, herbal formulations/medicines are completely not devoid of side effects/serious clinical consequences. Therefore complete clinical investigations of the herbal formulations must be encouraged in order to evidence any possible side effects.

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**REFERENCES**


terpenoid glycosides from Bacopa monnieri. Phytochemistry 66, 2719-2728


Satyavati GV, Raina MK, Sharma M (1976) Medicinal Plants of India (Vol I), Indian Council of Medical Research, New Delhi, 112 pp


Sumathi T, Devaraj SN (2009) Effect of Bacopa monniera on liver and kidney toxicity in chronic use of opioids. Phytomedicine 16, 897-903


Vijay V, Helen A (2010) Inhibition of pro-inflammatory mediators: Role of Bacopa monniera (Linn.). Wettest. Inflammation Research 59, 435-444

Vijay V, Kavitha SK, Helen A (2010a) Bacopa monniera Linn. Wettest inhibits type II collagen-induced arthritis in rats. Phytotherapy Research 24, 1377-1383


