

# A Comprehensive Review on the Ethno-Medicinal and Pharmacological Properties of *Bacopa monnieri*

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## ABSTRACT

*Bacopa monnieri* (L.), commonly known as Brahmi, is a medicinal plant it improves memory, regulates blood sugar levels, and contains many antioxidants that are essential to living a healthy life, it's often called a brain booster for its befitting effect on the brain and memory. The plant is used in Ayurveda and is known throughout the world for its numerous health benefits. The medical and pharmacological value of plant is increasing, plant extract gives there is enormous potential for it to reduce different inflammatory, depression, neuropharmacological, and other diseases. Several *in vitro* studies reveals that the plant extract phytochemicals helpful to treat human diseases in which free radical generation plays a significant role, and which needs more *in vivo* research. In this review elevated some potential pharmacological importance of bioactive components and its biological activity by some results of *in vitro* studies. Our studies also explained the phytochemicals from the plant extract involved *in silico* studies to find the potent therapeutic drug molecule to treat various diseases.

**Keywords:** *Bacopa monnieri* (L.), Anti-inflammatory activity, *in vitro*, *in silico*, Antioxidant activity, Anti-cancer activity.

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## INTRODUCTION

During thousands of years, the majority of people in the world have been depending on traditional medicine.<sup>[1]</sup> According to the World Health Organisation (WHO), 80% of the people in underdeveloped nations reportedly utilises traditionally used medicinal plants for their basic healthcare.<sup>[2]</sup> Herbal substances include a storage of bioactive substances through medicinal characteristics, which has been documented and used by numerous collections of people for the cure of various diseases over time.<sup>[3]</sup> A plant with medicinal applications has compounds that can be used therapeutically or that are substrates for the synthesis of important medicines in one or more of its tissues is considered to have properties. Many plants have been used in traditional medicine for a long time.<sup>[4]</sup> Even though some appear to be effective, there might not be sufficient scientific proof (such as results from double-blind tests) to support their effectiveness. In current years, more researchers focusing on plant research due to their enormous potential pharmacological value, research has been continuing on therapeutic plants.<sup>[5]</sup>

Brahmi (*Bacopa monnieri*) (L.) is an essential therapeutic herb in Ayurvedic medicine in India. It is a type of perennial herbaceous herbs called as 'Brahmi' that belongs to the Scrophulariaceae family. *Bacopa monnieri* (L.) is non-aromatic perennial, soft, creeping herb with succulent leaves.<sup>[6]</sup> It has multiple branches that grow particularly well in wet and marshy areas. This plant will grow to a height of 6 inches and has branches that climb horizontally covering the ground.<sup>[7]</sup> Green leaves with tiny marks are coin shaped grow and in the group of two or three alternately positioned on a hairy stem. Flowers are tiny, white and purple in colour, actinomorphic and emerge during the majority of the year it contains 4-5 petals. It is also known as a water aquarium plant because to its ability to grow in water. *Bacopa monnieri* (L.) is one of the oldest and most potent brain tonics utilised in the ayurvedic system from ancient times.<sup>[8]</sup>

The common names of *Bacopa monnieri* (L.) are hyssop, herb of grace and water hyssop. Traditionally the *Bacopa monnieri* (L.), used for memory enhancement, Central Nervous System (CNS), epilepsy, nerve tonic, anxiety, antidepressant, antioxidant activities and blood pressure.<sup>[9]</sup> The *Bacopa monnieri* (L.) plant extract is known for their important antioxidant activity, the research shown particularly the bacosides which are a class of bioactive compounds isolated from *Bacopa monnieri* (L.) shown results in animal study about develop antioxidant levels in the striatum, hippocampus, and frontal cortex of the brain.<sup>[10]</sup> Bacoside A has been found in experiments to protect against



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smoking-related cerebrovascular diseases by decreasing the amount of free radicals through its antioxidant capacity.<sup>[11]</sup> *Ali et al.*, 2021 worked a procedure for *in vitro* organogenesis, somatic embryogenesis, and plant regeneration using various explants of *Bacopa monnieri* (L.). Brahmi leaf resembles cerebellar structure, and this plant is best used in brain-related diseases that increase intelligence. Brahmi is an Ayurvedic medicinal plant that can be utilised to treat intestinal infections.<sup>[12]</sup>

### Bioactive compounds present in Brahmi (*Bacopa monnieri* (L.)) plant

*Bacopa monnieri* (L.) is an important Indian therapeutic plant used for numerous disorders, but is considerably known as a nootropic or brain tonic and memory enhancer. This annual plant has a variety of biologically active chemicals and is used as a replacement and complementary medicine in a number of countries.<sup>[13]</sup> The bioactive compounds present in plant like saponins, flavonoids, triterpenes, alkaloids, and cucurbitacin are may have an effect in neuroprotection.<sup>[14]</sup> A number of alkaloids present in the plant like a narcotine, brahmine, mannitol, herpestine, hersaponin, cucurbutacin, bacaposide and triterpenoid, saponins in this plant which are very effective for treat several human diseases.<sup>[15]</sup> *Bacopa monnieri* (L.) contains important secondary metabolites are bacosides A and B, D-mannitol, sapogenins, betulic acid, b-sitosterol, octacosane, amino acids nicotine, serine, a-alanine, aspartic acid, glutamic acid, herpestine, hersaponin, stigmaterol, brahmines, betulinic acid, b-sitosterol and stigmastenol (Table 1).

### Therapeutic properties of Brahmi (*Bacopa monnieri*) plant

*Bacopa monnieri* (L.) is an herb that has been used in traditional Indian medicine, in Ayurveda, using to treat anxiety, improve memory, as well as cardiac, respiratory, and neuropharmacological conditions like fatigue.<sup>[16]</sup> Various parts of *Bacopa monnieri* (L.) plant has been utilising as extracts that may exhibit anti-inflammatory and antioxidant abilities related to disorders including atherosclerosis, diabetes, and cancer<sup>[17]</sup> (Figure 1).

### Importance of *Bacopa monnieri* (L.) plant extract by Biological studies

The *Bacopa monnieri* (L.) plant extract has been using in research and most of the According to study, among other advantages, it may improve brain function and reduce stress and anxiety. A group of potent substances known as bacosides in *Bacopa monnieri* (L.) is trust to be response (Figure 2).<sup>[18]</sup> Antioxidants are bioactive compounds which help in the protection of cells from potentially harmful molecules known as free radicals. The majority of studies suggest an association between damage done by free radicals and numerous disorders, including heart disease, chronic diseases such as diabetes, and certain types of cancer.

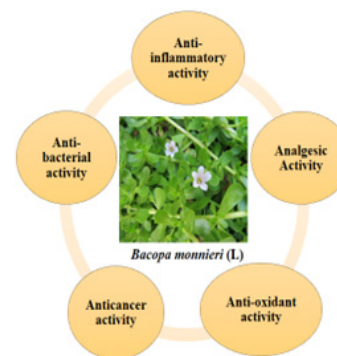
*Bacopa monnieri* (L.) contains potent compounds that may have antioxidant effects (Table 2).<sup>[19]</sup>

The compounds like bacosides, it has been shown that the primary bioactive elements of *Bacopa monnieri* (L.) will neutralise free radicals and prevent fat molecules from interacting with free radicals.<sup>[20]</sup> Lipid peroxidation is the process which takes place when fat molecules undergo a chemical reaction with free radicals. Lipid peroxidation is related to various diseases, including Parkinson's, Alzheimer's, and other neurodegenerative disorders, that for these benefits.<sup>[21]</sup>

### Anti-inflammatory activity

In this way, in taking of plants may protect against particular diseases whose aetiology involves immunological dysfunction or persistent inflammation by down regulating pro-inflammatory cytokines, COX, and lowering NF-kB translocation to the nucleus.<sup>[32]</sup> Also, plant bioactive qualities may decrease oxidative stress caused by an imbalance in the formation of Reactive Oxygen Species (ROS) and the ability of cell enzymes to serve as antioxidants. The anti-inflammatory effect of *Bacopa monnieri's* (L.) anti-inflammatory properties may also have neuroprotective properties. Central Nervous System inflammatory reactions (CNS) are generally discussed to as "neuroinflammation". Inflammation is a host immune response mechanism that protects against diseases, infections, and tissue injury.<sup>[33]</sup>

*Nemetchek et al.*, 2017 published research paper on *Bacopa monnieri* (L.) prevents the enzymes connected with inflammation in the brain and inhibits the produce of inflammatory cytokines from microglial cells. Thus, *Bacopa monnieri* (L.) can reduce CNS inflammation and suggests a prospective source of novel pharmaceuticals for the treatment of various CNS problems.<sup>[34]</sup> *Williams et al.*, 2014 documented that *Bacopa monnieri* (L.) has an anti-inflammatory effect on brain microglia. The study found that BM reduced NO and TNF-  $\alpha$  in stimulated RAW 246.7 macrophages and IFN- $\gamma$  in stimulated human blood cells. Furthermore, IL-10 levels in human blood cells were modestly raised, indicating a shift towards a regulatory T cell



**Figure 1:** Therapeutic activities of Brahmi (*Bacopa monnieri* (L.)) plant.

**Table 1: List of bioactive compounds in *Bacopa monnieri* (L.).**

Sl. No.	Compound names	Pubchem – CID
1.	D- Mannitol	6251
2.	Nicotine	89594
3.	Bacoside A	92043183
4.	Bacopasaponin A	101995276
5.	Bacopasaponin B	101996847
6.	Bacopasaponin C	21599443
7.	Bacopaside I	21599442
8.	Bacopasaponin F	16216038
9.	Bacopasaponin D	102000288
10.	Bacopaside II	9876264
11.	Bacopaside III	15922618
12.	Bacopaside IV	10865594
13.	Bacopaside V	11072737
14.	Bacopaside VIII	102080692
15.	Cucurbitacin B	5281316
16.	Betulinic acid	64971
17.	Plantainoside B	9847922
18.	Stigmastanol	5281703
19.	Cucurbitacin D	5281318
20.	Stearic acid	5281
21.	Rosavin	9823887
22.	3,4-Dimethoxycinnamic acid	717531
23.	Oroxindin	3084961
24.	Cucurbitacin E	5281319
25.	Brahmic acid	45272347
26.	Asiatic acid	119034
27.	Ascorbic acid	54670067
28.	Quercetin	5280343
29.	Stigmasterol	5280794
30.	$\beta$ -sitosterol	222284
31.	Ebelin lactone	15559069
32.	Bacopaside VI	11072737
33.	Triacotane	12535
34.	Apigenin	5280443
35.	Octosane	356
36.	Heptacosane	11636
37.	Stigmastanol	5280794
38.	Bacosterol	5281326
39.	Loliolide	100332
40.	Asiaticoside	24825675
41.	Luteolin	5280445

Sl. No.	Compound names	Pubchem – CID
42.	Ursolic acid	64945
43.	Dotriacontane	11008
44.	Nonacosane	12401
45.	Hentriacontane	12410

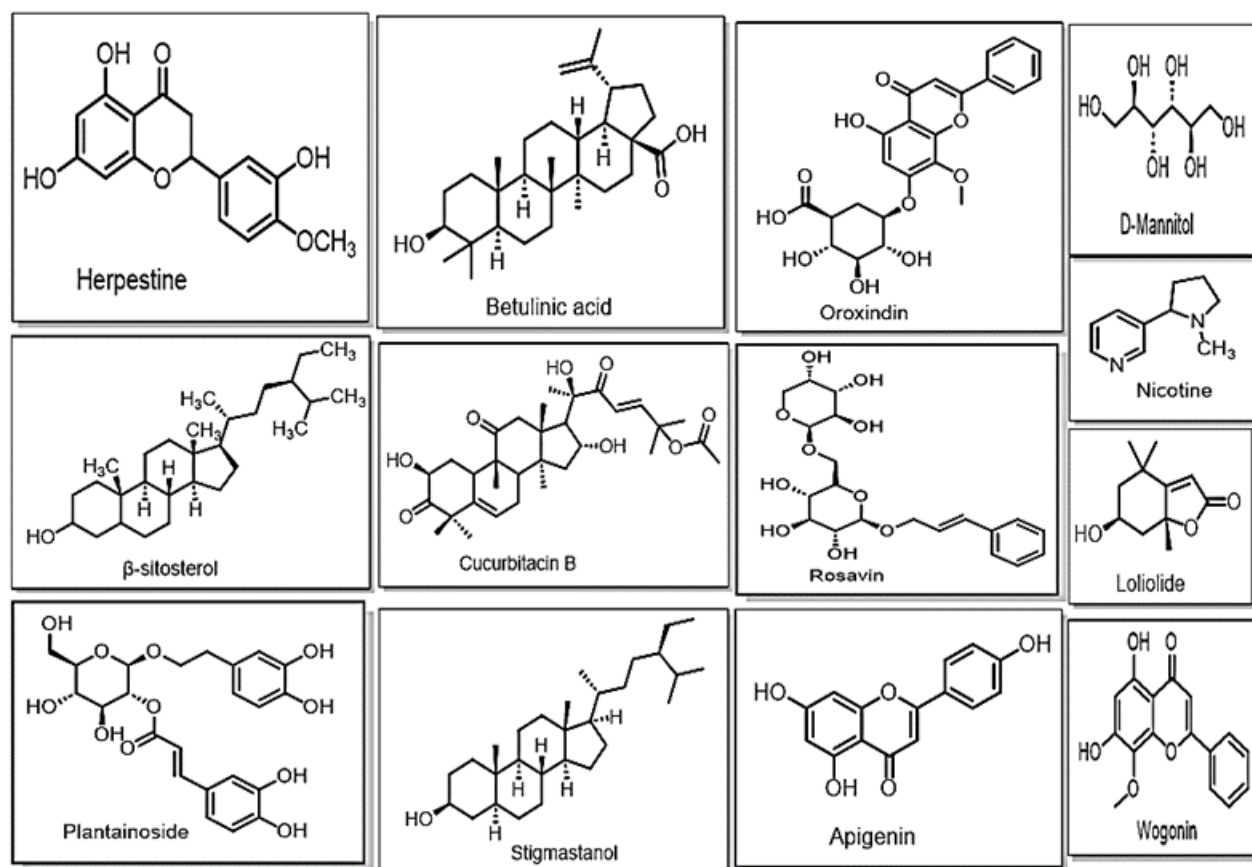
phenotype.<sup>[35]</sup> *Jeyasri et al., 2022* worked on a research paper to identify bioactive phytochemicals from *Bacopa monnieri* (L.) that be able to be working to regulate the gene targets associated to Signaling pathways, which could eventually main to the treatment of inflammation-reactive diseases. The results show that gained *in vitro* results and revealed that the recognised bioactive phytochemicals capably inhibit the expression of inflammation-responsible genes such as COX2 and iNOS in LPS-induced RAW264.7 cells.<sup>[36]</sup>

### Analgesic Activity

The acetic acid-induced writhing method is a method for assessing analgesic activity in mice that exhibits noxious stimulation in mice. *Siraj et al., 2013* reported analgesic activity of the ethanol extract of the whole plant of *Bacopa monnieri* (L.) the acetic acid-induced writhing model in mice was used to validate the result. The polar compounds existing in the plant extract may be accountable for the obtained analgesic activity. And the result shown it can be concluded that the ethanol extract of *Bacopa monnieri* (L.) possesses analgesic activity.<sup>[37]</sup>

### Antioxidant activity

Numerous studies reviewed the Indian medicinal plant *Bacopa monnieri* (L.) as a dietary antioxidant, with *in vivo* and *in vitro* research have revealed many mechanisms of action that may protect the brain against oxidative damage. It also reduces the risk of free radical oxidation.<sup>[38]</sup> *Bacopa monnieri* (L.) is a possible medicinal antioxidant to reduce oxidative stress and progress cognitive function and inhibit the toxicity of kidney and morphine induction liver in rats, Diabetes induced caused modulation in SOD activity, the researchers found antioxidant levels improved through bacoside-A.<sup>[20]</sup> *Sharath et al., 2010* the methanolic extract of *Bacopa monnieri* (L.) and its isolated bioactive compounds were studied in this bacoside A is demonstrated wound-healing activity that was reflecting. The results obtained show that *Bacopa monnieri* (L.) may have a significant impact on the treatment of human diseases in which the production of free radicals is important.<sup>[39]</sup> The SNP was regulated by pre-treatment with *Bacopa monnieri* (L.) plant extract-induced upregulation of cytochrome c, Bax, and caspase 3 expression, as well as down-regulation of Bcl-2 expression, by maintaining mitochondrial integrity advisable cytoprotective function of extract towards SNP-caused damage.<sup>[40]</sup> *Russo et al., 2003* publication shows the extract of *B. monnieri* (L.) plant exhibits effective adsorption and neutralisation of free radicals by

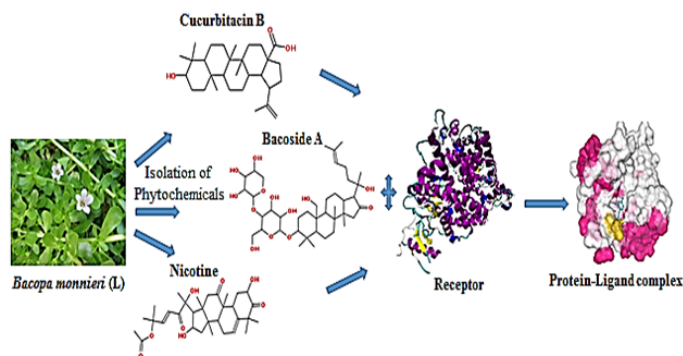


**Figure 2:** The major bioactive compounds of *Bacopa monnieri* (L.).

absorbing singlet oxygen or degrading peroxides are examples of antioxidant activity. It has been shown that upon superoxide radical activation, glial cells create NO (Nitric Oxide) via an enzyme-independent process.<sup>[41]</sup> Radhika Kapoor *et al.*, 2008 published the research paper the study was initiated to assess the preventive effect of the medicinal herb *Bacopa monnieri* (L.) on tissue antioxidant defence system and lipid peroxidative condition in diabetic rats treated with streptozotocin. The study concluded *Bacopa monnieri* (L.) could be accountable for the restoration of metabolic properties and according to protection against streptozotocin-induced diabetic rats.<sup>[42]</sup>

### Anti-cancer activity

The primary cause of cancer is cellular instability and the suppression of apoptotic mechanisms, which results in tumour cell proliferation and accumulation.<sup>[43]</sup> The disease's possibilities for therapy have been limited, and research is being conducted to determine the best possible method for treating cancer with medicinal plants and herbs. Another approach is used to decrease the adverse effects induced by using them for an extended period of time.<sup>[44]</sup> There are various plants that induce programme death cell (apoptosis) in cancer cells, the most of plant extracts have been shown to have significant effects on the same. p53 was the first tumour suppressor gene revealed to be associated with apoptosis, this gene is frequently mutated in tumours.<sup>[45]</sup>



**Figure 3:** *In silico* studies of bioactive compounds in *Bacopa monnieri* (L.).

Recent research has suggested that it may be useful in cancer prevention and treatment. The majority of a study of the effects of *Bacopa monnieri* (L.) extracts obtained from simulated digestive juices on physiological characteristics of prostate cancer cells (DU 145), such as survival and migratory activity, are reported in the paper.<sup>[46]</sup> In *Vibrio harveyi* mutagenicity experiments, the protective profile and chemopreventive effects of *Bacopa monnieri* (L.) extracts were studied.<sup>[47]</sup> *Bacopa monnieri* (L.) is the anticancer effect of ethanolic fraction has previously been described by Mallick *et al.*, 2015 as a possible source of anti-cancer lead compounds. The results of this study will enable us to develop a bioactive compounds extraction processes that has a cytotoxic effect on breast cancer cell lines MCF7. This particular

**Table 2: List of important bio active compounds in *B. monnieri* (L.) and its biological activity.**

Sl. No.	Name of the compounds	Biological activity
1.	Betulinic acid	Inhibition of Human Immunodeficiency Virus (HIV), antimalarial, anti-inflammatory, antibacterial, anthelmintic and antioxidant properties. <sup>[22]</sup>
2.	Loliolide	Exhibit a variety of physiological activities, including phytotoxic, antitumor, and growth-inhibiting activities for plants, as well as antitumor and antimicrobial behaviours for animals and microbes. <sup>[22]</sup>
3.	D- Mannitol	Mannitol actually helps avoid water loss and balance salt accumulation without interfering normal metabolism. It also has been postulated to act as scavengers of reactive oxygen species and therefore may be helpful in preventing lipid peroxidation that causes cell damage. <sup>[23]</sup>
4.	Bacoside I	Inhibited the spread of breast cancer cells and had anti-cancer action against several cancer cells, including those in the lung, prostate, brain, and colon. <sup>[24]</sup>
5.	$\beta$ -sitosterol	The Compound recognised to have the finest antimicrobial activity. <sup>[25]</sup>
6.	Cucurbitacin B	According to reports, cucurbitacins activate both the JAK/STAT3 pathway and the MAPK pathway to cause apoptosis. By inhibiting cyclins, cucurbitacins may prevent the cell cycle from occurring. Additionally, they accelerate autophagy and prevent cancer cells from migrating and invasion. <sup>[26]</sup>
7.	Apigenin	Active as an antioxidant, neuroprotective, anti-inflammatory, anti-amyloidogenic, and cognition-enhancing substance with stimulating potential in the treatment/prevention of Alzheimer's disease. <sup>[27]</sup>
8.	Rosavin	Traditionally using as adaptogens, antidepressants, and anti-inflammatory remedies. <sup>[28]</sup>
9.	Wogonin	It's showing antiviral, anti-inflammatory, anticancer, and antioxidant effects. <sup>[29]</sup>
10.	Oroxindin	Antitumor, Anti-inflammatory, antioxidant. <sup>[30]</sup>
11.	Stigmastanol	Anti-inflammatory and immunomodulatory activities. <sup>[31]</sup>

group of substances can be utilised in future studies to develop novel chemotherapeutic substitutes for breast cancer patients.<sup>[48]</sup> Through *in silico* and *in vitro* experiments, the majority of the studies examined the inhibitory effects of *Bacopa monnieri* (L.) extract on signalling pathways associated in prostate cancer. Bacosides downregulated different signaling pathways and may be cytotoxic to prostate cancer.<sup>[49]</sup> Compounds in *Bacopa* can significantly human breast cancer cell line prevention migration, adhesion, and invasion of MDA-MB-231,<sup>[50]</sup> thereby reducing the growth, spread, and metastasis of breast cancer. Bacoside A, the active compound of can also be effective in preventing some forms of liver cancer.<sup>[51,52]</sup> *Bacopa monniera* (L.) extracts cause apoptosis (programmed cell death) of sarcomas in animal studies of cancer.<sup>[53]</sup>

### Anti-bacterial activity

The leaves extract of plant can show possible antibacterial activity due to the occurrence of different phytochemicals, such as phytosterols, flavonoids, alkaloids, phenol, saponin, and tannins.<sup>[54]</sup> Antibacterial activity of Bacoside A an active component extracted of *Bacopa monnieri* (L.) is before been reported. Bacoside A and the methanolic extract revealed a significant zone of inhibition against the clinical strain of *Staphylococcus aureus*.<sup>[55]</sup> The majority of the action is demonstrated by *Bacopa monnieri* (L.) EtOAc extracts and MeOH, followed by benzene, aqueous, and petrol extracts; this herb has also been proposed for clinical benefit in several pathogenic conditions. According to the research, almost all of the bioactive substances identified in these plant extracts could be employed in the creation of new antibacterial medicines.<sup>[56]</sup> As a result, harmful bacteria are known to acquire antibiotic resistance, making the search for new medicines an ongoing effort. *Bacopa monnieri* (L.) may be active for treatment in changed pathogenic diseases.<sup>[57]</sup>

### Importance of *Bacopa monnieri* (L.) plant extract by *in silico* studies

Traditional research on medicinal herbs has grown in prominence in recent years, because of essentially to the natural sources and variety of such plants, which enable them to enhance contemporary pharmaceutical treatments.<sup>[58]</sup> As computer technology has advanced, *in silico* approaches like as virtual screening and network analysis have been frequently applied in efforts to understand the pharmacological foundations of traditional medicinal plant application.<sup>[59]</sup> The application of virtual screening and networked pharmacology in the creation of new drugs can identify active molecules among alternatives and effectively clarify the process of action of medicinal plants.<sup>[60]</sup> *Bacopa monnieri* (L.) has been conventionally known to be applied to treat dissimilar disorders. Therefore, in current review elevating an *in silico* based study was describe the pharmacological effect of *Bacopa monnieri* (L.) in different diseases by using its bioactive compounds (Figure 3).

Sangeet *et al.*, 2022 worked on research paper *in silico* study of *Bacopa monnieri* (L.) the bioactive compounds for drug improvement against neurodegenerative disorders and the results, gives an *in silico* methodology toward appreciative the anti-neurodegenerative property of *Bacopa monnieri* (L.) phytochemicals and demonstrates the significance of four key phytochemicals as a replacement for manufactured medicines in the treatment of many neurodegenerative disorders shows the significance of four key phytochemicals as an alternative for manufactured medicines in the treatment of many neurological disorders.<sup>[61]</sup> Ramasamy *et al.*, 2015 Bacoside - A, Aglycones, and their derivatives were studied *in silico* and *in vitro* as the constituents responsible for the cognitive benefits of *Bacopa monnieri* (L.). A combination of *in silico* and *in vitro* tests displayed that the bacoside aglycone derivative, ebelin lactone, has better CNS drug-like and receptor-binding capabilities than the reference compound. The outcomes of such investigations will provide a better indication of *Bacopa monnieri* (L.) potential for the therapeutic use of aglycones and their derivatives.<sup>[62]</sup> Roy *et al.*, 2019 published the paper molecular docking studies were used to identify bioactive substances found in *Bacopa monnieri* (L.), against Caspase-3 and Tau protein kinase I to prevent Alzheimer's disease. They used approximately the docking binding affinity value prediction in an *in silico* investigation revealed that among 17 natural compounds selected from *Bacopa monnieri* (L.), two saponins demonstrated good binding ability. On CASP-3 and TPK I receptors, Bacopasaponin G and Bacopasaponin N2 had a lower binding energy value than Donepezil.<sup>[63]</sup> The research shows that medicinal property of *Bacopa monnieri* (L.), the computational studies conducted for the extraction of bioactive compounds exposes the phytochemicals' natural medicinal nature and their potential to act as a therapeutic candidate to treat different diseases.<sup>[64,65]</sup>

## CONCLUSIONS

*Bacopa monniera* (L.), is an ancient Ayurvedic plant that has been used for centuries as an anti-antipyretic, inflammatory, memory enhancing, analgesic, cancer, bacterial, oxidant, sedative and antiepileptic agent. Several laboratories have thoroughly researched the plant, extract, and extracted bacosides (the principal active components) for their diverse biological activities. Furthermore, cardio tonic, anti-inflammatory, and other pharmacological properties of *Bacopa monnieri* (L.) preparations/extracts have been studied. Therefore, in view of the important activities performed by this plant, research is an ongoing process over *Bacopa monnieri* (L.). Most of the studies theorises that *Bacopa monnieri* (L.) and their bioactive compounds with other substances, as suggested by Ayurvedic and modern medicine systems, may result in synergistic effects requiring further research.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

## ABBREVIATIONS

**WHO:** World Health Organization; **CNS:** Central Nervous System; **ROS:** Reactive Oxygen Species; **SOD:** Superoxide dismutase; **NO:** Nitric Oxide; **HIV:** Human Immunodeficiency Virus; **MAPK:** Mitogen-activated protein kinase; **COX2:** Cyclooxygenase 2; **iNOS:** Inducible nitric oxide synthase; **LPS:** Lipopolysaccharide; **TNF-  $\alpha$**  - Tumor necrosis factor alpha; **IFN- $\gamma$** : Interferon gamma; **NF- $\kappa$ B:** Nuclear factor kappa.

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