Review

Phytochemical Composition and Pharmacological Properties of *Bacopa monnieri*

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Review

Phytochemical Composition and Pharmacological Properties of *Bacopa monnieri*

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Abstract

Plants have always been an indispensable part of human life since the beginning of human civilization. *Bacopa monnieri* (L.), popularly known as Brahmi, is widely considered as the water hyssop or Indian pennywort. In Ayurveda, it is classified as a Rasayana (rejuvenation) and projected to promote mental and physical health, rejuvenate the body in debilitated conditions and increase longevity. Each naturally synthesized chemical constituent identified from *Bacopa monnieri* leaf extract with different solvents, has significant pharmacological activity. Multiple preclinical and clinical studies have supported the neuroprotective, hepatoprotective, gastroprotective, antioxidant, antitumor, learning and memory enhancing activity of *Bacopa monnieri* and its bioactive constituents. The present review describes the botany, pharmacology, traditional uses, phyto-constituents of *Bacopa monnieri* to highlight future research needs and potential uses of this medicinal herb.

Keywords: antioxidant; anti-tumour; bacoside; *Bacopa monnieri*; pharmacological activity

1. Introduction

Bacopa monnieri (L.) commonly known as "Brahmi" or "Jalanimba" is an important medicinal herb of immense importance quoted in ancient Indian literature. Genus *Bacopa* mainly consists of 70-100 aquatic plants commonly known as Water Hyssop by virtue of its related appearance (Sharma et al., 2015; Aasim et al., 2019a, 2019b; Abdulminam et al., 2017) (Figure1.). *Bacopa monnieri* belongs to family Scrophulariaceae (also known as Plantaginaceae), is a non-aromatic nootropic medicinal herb used in Ayurveda (Asim et al., 2019; Darokar et al., 2001). It is also known as, *Herpestis monniera*, or Indian pennywort (Devendra et al., 2018). In India, it is commonly referred as 'Brahmi or Jalanimba'. The common name *Brahmi* is derived from the word 'Brahma' who is referred to the maker of the universe in the Hindu religion (Prasad et al., 2008). Brahmi, has another meaning of bringing knowledge of the leading truth (Mukherjee et al., 2011). The 'Charaka Samhita' a very well known Ayurvedic treaty has recommended this herb in curing the variety of brain-related symptoms such as anxiety, poor cognition, epileptic disorder and lack of concentration, as a diuretic and as an energiser for the nervous system and the heart (Dhanasekaran et al., 2007). In ancient Indian literature, this herb is very well known for its practical advantages over mental disorder with no side effects. It is also known as nootropic plant by the ancient personalities (Bhardwaj et al., 2016). It helps in improving the speed of visual information processing (Pase et al., 2012; Stough et al., 2008).

The drugs which are involved in enhancing brain activity such as improving Nootropic herbs and drugs are those which are used in various activity: memory, mood, and various other symptoms which deals with the mental dis-functioning are called as nootropic drugs and here are some examples of herbs which have a nootropic activity that is Ashwagandha (*Withania somnifera*), Shankhpushpi, Ginkgo (*Ginkgo biloba*) and Gotu kola (*Centella asiatica*) and *Brahmi* (*Bacopa monnieri*) (Devendra et al., 2018). *Brahmi* has been categorized as a "Medhyarasayana", in Ayurveda as this drug is meant to be useful in improving memory and various other factors related to memory such as maturing, development and growth. This herb is also useful in providing consolation to those who

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suffer from disorders such as anxiety or epilepsy (Sangwan et al., 2017; Tripathi et al., 2020; Srivastava et al., 2020; Zuo et al., 2017; Prakash et al., 2017; Hosamani et al., 2016). A Report given by ancient scientist for more than 3000 years reflects its pivotal role in neurological disorders as well as when the extract from this plant was used it showed its useful efforts in various seen symptoms against inflammatory, pyretic, depressant, microbial and cancer (Bhardwaj et al., 2016). *Bacopa monnieri* is recognised for reinvigorating and cognitive enhancing activity in Ayurveda as it makes sharper memory and ability of reasoning and understanding objectively (Pandareesh et al., 2015; Sukumaran et al., 2019; Kumar et al., 2016; Mitra- Ganguli et al., 2017; Pham et al., 2019; Dethe et al., 2016).

According to the reports, it is assumed that Bacosides are actively involved in fixing up dead neurons by improving the activity of the kinase and the synthesis of neurons that are attached to the restoration of synaptic activity. Thus, these compounds are also involved in the enhancing of the nerve impulse in a body (Simpson et al., 2019). The main feature of *B. monnieri*, which drags everyone's attention towards this medicinal herb, is the ability to enhance and developing memory (Pandareesh et al., 2015).

It not only enhances memory power but also has various other properties due to which it may be a remedy for various serious diseases such as Alzheimer's disease, cancer, anxiety, epileptic, gastrointestinal effects, and depression (Chaudhari et al., 2017; Smith et al., 2018; Murugaiyan and Bhargavan, 2020; Komali et al., 2020; Nakashima et al., 2016; Girish et al., 2016).

2. Research Methodology and Source Selection

This review is prepared by searching selected publications related to Pharmacological properties, geographical distributions and chemical constituents of an important medicinal plant *Bacopa monnieri.* Most of these publications are selected by screening of literatures in PubMed (https://pubmed.ncbi.nlm.nih.gov/), Springer (https://link.springer.com/), Scopus (https://www.scopus.com/home.uri), Science Direct (https://www.sciencedirect.com/) and some are extracted from Google scholar search engine. Research articles and Review publications between 2000 to 2025 were used to cover this review. The structures of bioactive constituents of *Bacopa monnieri* were extracted from PubChem database (https://pubchem.ncbi.nlm.nih.gov/). Moreover, references of selected articles were also screened manually for additional information.

3. Plant Description and Morphology

Bacopa monnieri (BM), is a small, creeping, somewhat succulent herb which is known to have leaves and flowering stems that are up to 11-30 cm in length that are grown from the stems which creep and later modify themselves as roots that arise from nodes (Vishwakarma et al., 2016). The leaves seem to be simple, obovate-oblong, opposite, approximately up to 2 cm × 1 cm, with entire margins, and the flowers are up to 0.6-3 cm in length, that is usually long as compared to the leaves and maybe blue or white having the different purple-colored veins in the plant (Thorat et al., 2018). The corolla of this plant is five-lobed in white or pinkish in colour with purple blotches. The fruit, as reported by the researchers, is a capsule that is up to 5 mm and thus later modifies in the constant calyx (Vishwakarma et al., 2016). The plant is a little bit bitter in taste, without having any kind of odour as well as it is found to be succulent herb when fresh but it becomes shriveled on drying. The shapes of dried primary roots are found to be cylindrical in a somewhat off-white colour with an approximately 5 mm in diameter (Figure 1) (Devendra et al., 2018).

Figure legends:

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Figure 1. Bacopa monnieri.

4. Habitat and Geographical Presence of the Plant

Bacopa monnieri is a perennial, creeping or prostrate herb with numerous branches commonly grows in the area having wet soil, shallow water, and marshy places. This plant grows well in poorly drained acidic soils. This herb is mainly found at elevations from sea level to altitudes of 4,400 feet and thus can be easily cultivated in an inadequate amount of water. The Flowers and fruit of Bacopa appear in summer, and the entire plant is used for medicinal purposes (Jain et al., 2017). Specifically, this herb grows in the marshy areas of southern India, Asia, Europe, Africa, Australia, and South America (Dang et al., 2018). It is also found in Vietnam, Florida, southern part of United States (Figure 2.).

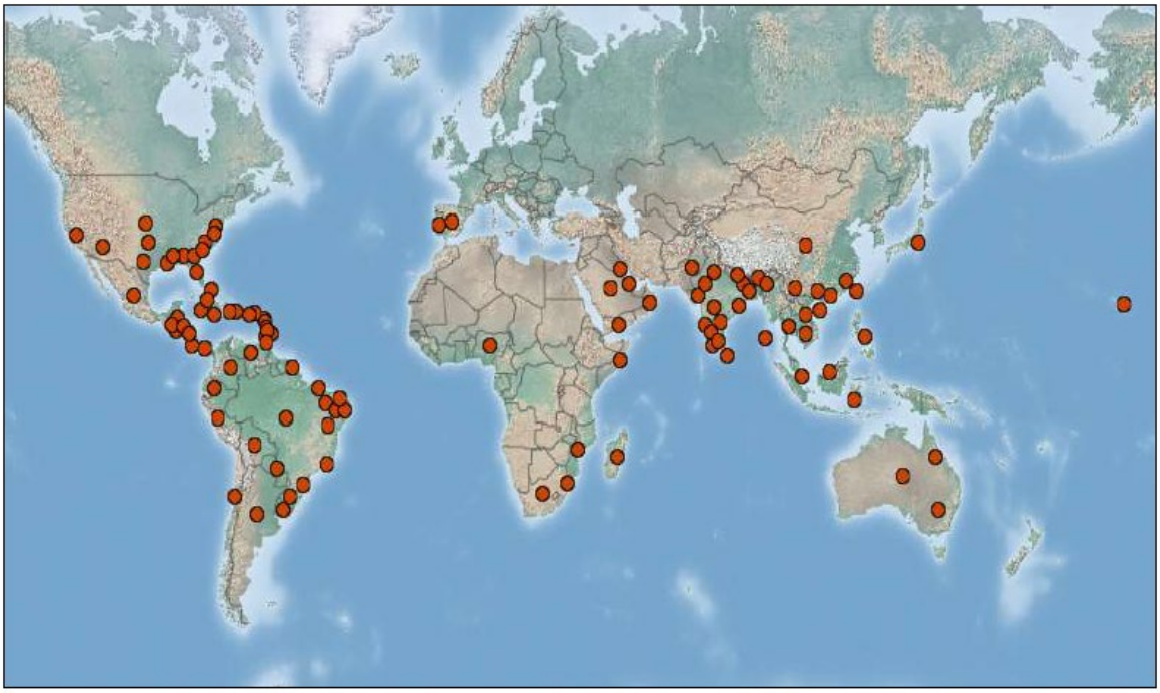

Figure 2. Geographical distribution of *Bacopa monnieri.*

5. Chemical Constituents

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B. monnieri has several pharmacological activities as it has many useful chemical constituents. It contains about 88.4% of moisture including carbohydrates, fat, protein and minerals in plant (Thorat et al., 2018). This herb contains a broad range of biologically active components such as triterpenoidal saponins, alkaloids, flavonoids, glycosides, and cucurbitacins (Bhandari et al., 2020; Ohta et al., 2016) (Figure 3.).

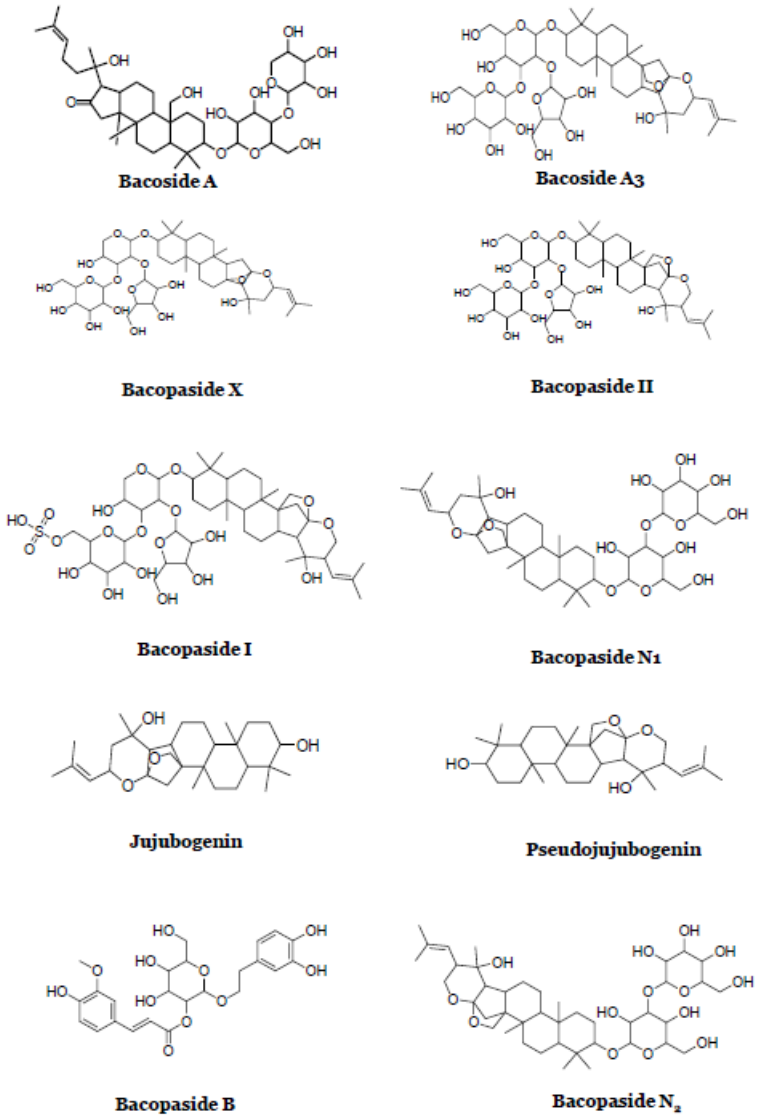

Figure 3. Major constituents of *Bacopa monnieri* and their structures.

5.1. Major

Bacoside A: The major constituents in *Bacopa monnieri* are brahmine, herpestine, alkaloids, and saponins. The saponins are considered as bacoside A, bacoside B, and betulic acid (a) and (b). D-mannitol, stigmastanol, β-sitosterol, and stigma sterol, bacoside A. On acid hydrolysis bacoside A formed the 3 sugars, in which 2 were found as glucose and arabinose when bacoside B was undergone hydrolysis it also gave glucose and arabinose (Jain et al., 2017).

5.2. Minor

Bacoside B, bacoside A1, bacoside A3, bacogenin A1, bacogenin A2, bacogenin A3, bacogenin A4, bacopa saponin-C, bacopasides I and II, bacopasides III-V, bacopasides VI-VIII, bacobitacins A-D, monnieraside I, monnieraside III, monnieri, plantioside B; jujubogenin, pseudojujubogenin, 3-O-β-D-glucopyranosyl-(l—»3)-[β-Dglucopyranosyl] jujubogenin, 3-O-[β-D--glucopyranosyl-(l—»3)-[β-Dglucopyranosyl] pseudojujubogenin, betulinic acid, wogonin, oroxidin, luteolin, luteolin-7-

 doi:10.20944/preprints202507.0981.v1

glucoside, luteolin-7-glucuronide, apigenin- 7-glucuronide; nicotine, 3-formyl-4-hydroxy-2H-pyran, bacosine, bacostcrol, bacosterol-3-O-β-D-glucopyranoside, stigmasterol, stigmastanol, β-sitosterol, D-mannitol, and an uncharacterized glycoside (Jain et al., 2017)..

Bacogenins are formed from Bacoside A on acid hydrolysis. Bacoside B is different from Bacoside A in terms of optical rotation. Bacoside A is laevorotatory, whereas Bacoside B is dextrorotatory. The Bacoside A is formed from four Higlycoside which are Bacoside A3, Bacoside, Jujubogenin. The 4 diglycos are Bacoside N1, Bacoside N2, Bacoside 4 and Bacoside 5 are included in the Bacoside B (Jain et al., 2017).

6. Pharmacological Properties of Bacopa Monnieri

Bacopa monnieri has been proved a "boon" in Ayurvedic medicine as it contains many beneficial components. It has been used in several medicines for the cure of many fatal neuro-diseases like Parkinson's diseases, Alzheimer's as well as show antiepileptic, anti-anxiety, anti-depressant, antioxidant, memory enhancer etc. (Singh et al., 2020; Dubey Chinnathambi, 2019; Komali et al., 2018; Sudershan et al., 2018; Zu et al., 2017; Promsuban et al., 2017) (Figure 4.). It has been well studied that, complete plant, especially the dried leaf extract has great medicinal significance in indigenous medicine. In the traditional system of Indian medicine, *Bacopa monnieri* is well considered as a drug to enhance memory functions and to overcome the effects of mental stress (Hazra et al., 2017). It is also used in the treatment of skin disorders, gastrointestinal infections, epilepsy, pyrexia, analgesia and rejuvenation (Shamu et al., 2020; Komali et al., 2020; Fawad et al., 2018; Yoon and Lee, 2017; Nemetchek et al., 2017). *Bacopa monnieri* extract is also familiar to have potent antioxidant and anticancer properties (Jauhari et al., 2019; Sarkar et al., 2019) Due to affluent active components, the plant has been utilized mainly as a nootropic digestive attention and for improving respiratory functions (Chaudhari et al., 2017; Haque et al., 2017). We will further discuss some critical pharmacological properties of *Bacopa monnieri* in detail.

6.1. Neuroprotective Activity

In recent years, an enriched extract of bacosides from *Bacopa monnieri* is well formulated and marketed in India under the trade names like Memory plus, BacoMind™ and KeenMind (Pase et al., 2012). *Bacopa monnieri* extract is best known for its use as a memory enhancer and neural tonic (Kongkeaw et al., 2014). The molecular mechanism of the neuroprotective activity of bacosides is principally associated with the regulation of mRNA translation and surface expression of neuroreceptors (Sekhar et al., 2019). Recent studies suggest that *Bacopa monnieri* functions by inhibiting acetylcholinesterase activity or by activating choline acetyltransferase, thereby increasing the cerebral blood flow. It also functions in beta-amyloid reduction and modulation of neurotransmitters like dopamine, acetylcholine and 5-hydroxytryptamine (Ahirwar et al., 2012; Aguiar and Borowski, 2013). *Bacopa monnieri* extract acts as a potent nutritional antioxidant, with a unique mechanism of action to protect the brain from oxidative damage and age-related cognitive disorders such as dementia and Alzheimer's disease (Witter et al., 2018; Saini et al., 2019). *Bacopa monnieri* could play a protective role against Alzheimer's disease by modulating the function or expression of Na^+, K^+-ATPase (Liu et al., 2013). Various studies utilising the standardised CDRI08 enriched leaf extract have shown that extract of *Bacopa monnieri* improves cognitive function mainly in the elderly (Nathan et al., 2004). Several *in vivo* studies have suggested that *Bacopa monnieri* extract enhance the defence system against oxidative stress by reducing the accumulation of free radicals in the brain (Shinomol, 2011). Saponin rich extracts of this plant have showed the dose associated enhancement in enzymatic activity of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxide (GSH-Px) (Bhattacharya et al., 2000). The bacosides present in *Bacopa monnieri* has the ability to enhance nerve transmission, cell proliferation, neuroblast differentiation, repairing damaged neurons by modulating kinase activity and increasing new protein synthesis in brain (Prasad et al., 2008; Kwon et al., 2018).

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6.2. Anti-Tumour Activity

Recent studies have indicated the potential aspect of *Bacopa monnieri* in cancer treatment and prevention. *Bacopa monnieri* plant extracts found to have strong cytotoxic effect in lung, colon and breast cancer (Mallick et al., 2015; Pei et al., 2016). Bacopaside II was believed to inhibit the growth of colon cancer by inducing cell cycle arrest and apoptosis (Smith et al., 2018). Also, the extract containing a high amount of bacoside A has very strong antimutagenic activity against nitroquinoline-N-oxide, which significantly reduced cancer cell motility (Koczurkiewicz et al.,2017). Cucurbitacins and betulinic acid present in *Bacopa monnieri* has been reported for their strong anti-tumorigenic effect by promoting cell cycle arrest at G2/M phase and inhibit the formation of aggregated cells (Mallick et al., 2015). The *in-vitro* study suggests that the anticancer property of bacoside extracts from *Bacopa monnieri* might be due to the inhibition of DNA replication in cancerous cell (Aithal and Rajeswari, 2019).

6.3. Antioxidant Activity

Oxidative stress (OS) is involved in the pathogenesis of several diseases including cancer, neurodegenerative diseases, cardiovascular diseases, lung diseases, kidney fibrosis, metabolic syndrome, diabetes, etc (Upadhyay and Srivastava, 2019) (Figure 5.). Several studies have shown that *Bacopa monnieri* extract has potent antioxidant activity (Prasad et al., 2013; Gupta et al., 2019). Based on the previous studies, bacosides were found to have a potent antioxidant effect (Waly et al., 2019). The bacoside rich extract was found to regulate the expression of several enzymes involved in scavenging and production of reactive oxygen species (ROS) (Sekhar et al., 2019). Recently, a report showed that bacoside II and bacoside A3 had increased cytoprotective ability towards oxidative stress due to its functional role in decreasing intracellular ROS (Bhardwaj et al., 2019). *Bacopa monnieri* extracts modulate the activities of CYP450 dependent enzymes, HSP70 and SOD which provide protection under adverse stress conditions (Murugan and Bhargavan, 2020). Aqueous extract of *Bacopa monnieri* conferred geno-protection by reducing the nicotine-induced lipid peroxidation (Tousson et al., 2019).

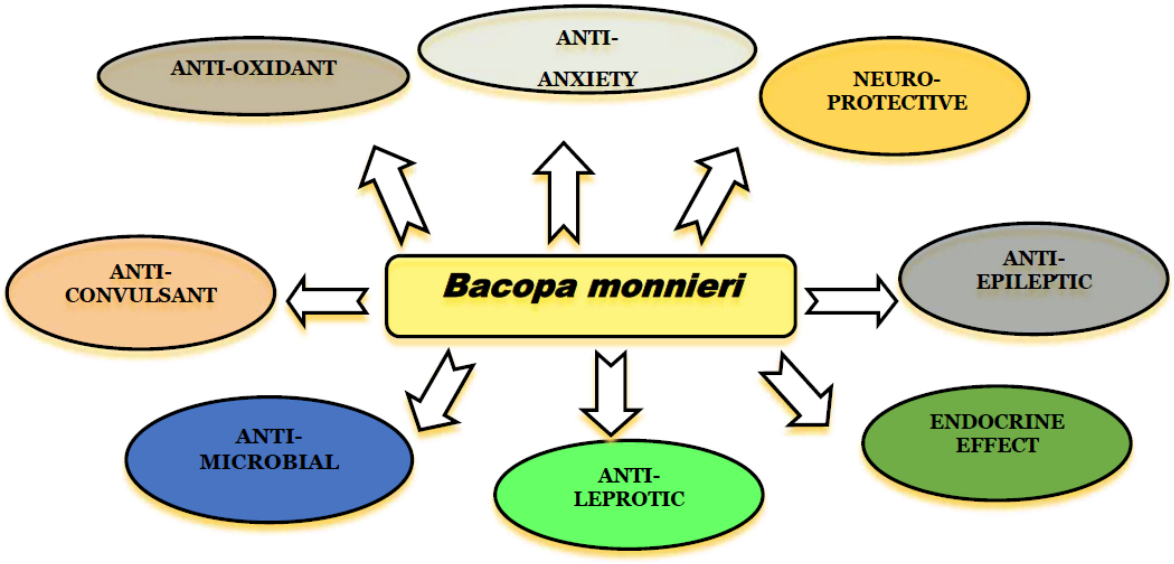

Figure 4. Major pharmacological activities of *Bacopa monnieri.*

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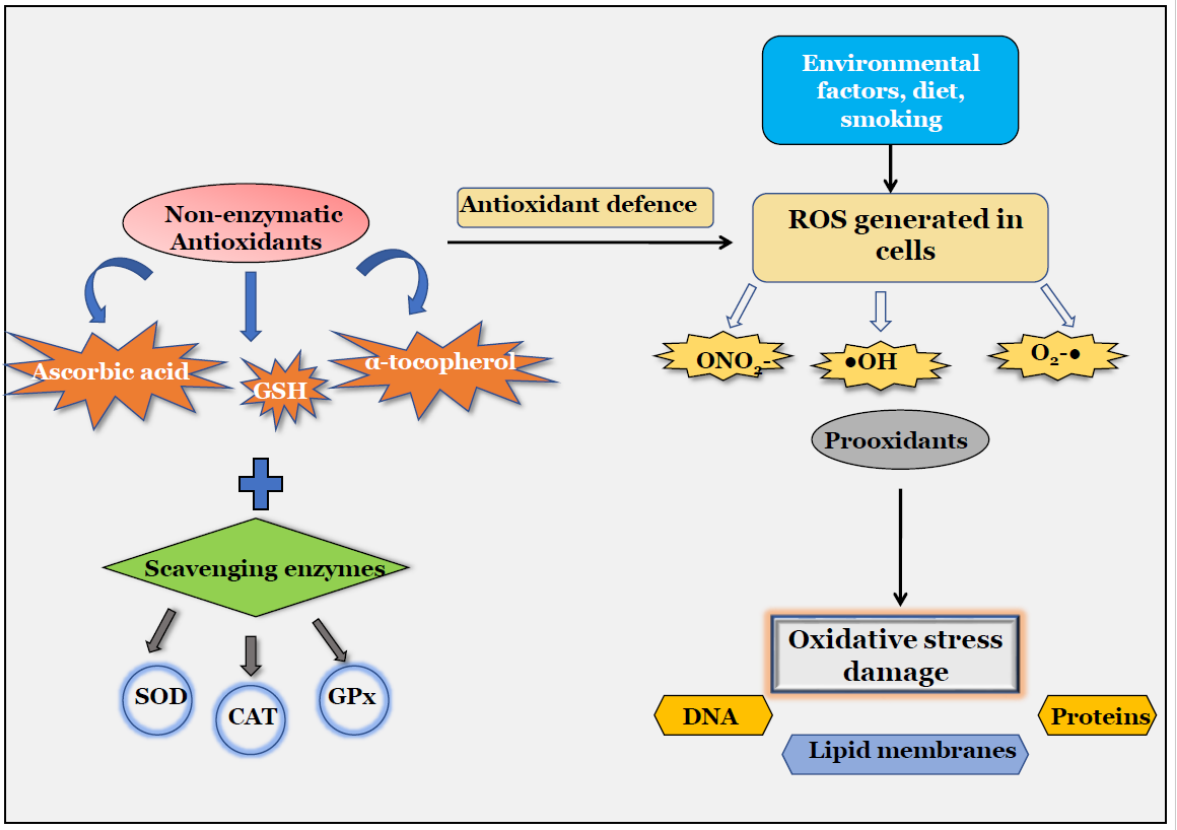

Figure 5. Oxidative Stress Mechanisms.

6.4. Gastroprotective Activity

Various *in-vivo and in-vitro* studies have suggested that *Bacopa monnieri* might play a crucial role in protecting gastric ulcers (Akbar, 2020). Caffeic acid by-products from *Bacopa monnieri* plants act as a potent inhibitor of pancreatic lipase activity (Rehman et al., 2019). The main active components like plantainoside B and desrhamnosyl isoacteoside extracted from *Bacopa monnieri* show reduced plasma triglyceride levels (Nakashima et al., 2016). The plant extract was shown to have antibacterial activity against *Helicobacter pylori* which is mainly subjected to chronic gastric ulcers (Goel et al., 2003). The bacosides present in the plant extract has potent antiulcerogenic properties which significantly strengthen the mucosal barrier and decrease mucosal exfoliation (Dharmani and Palit, 2006; Dorababu et al., 2004; Sairam et al., 2002; Rao et al., 2000).

6.5. Hepatoprotective Activity

Bacopa monnieri extracts possess the hepatoprotective activity, and they were active against hepatotoxicity induced by a range of chemicals such as carbon tetrachloride, alcohol and drugs (Rifampicin, paracetamol, isoniazid). Bacoside-A was assessed as the principal constituent of *Bacopa monnieri* extract followed by bacopaside-II and bacopasaponin-C (Padmanabhan and Jangle, 2004; Karim et al., 2020). The treatment with this extract restored histopathological changes in liver cells and also lowered the elevated enzymes such as serum AST, ALT and creatinine (Shahid et al., 2016). Chronic hepatitis, cirrhosis and fatty liver disease are caused due to consumption of alcohol metabolism in the liver due to generated RNS and ROS. The administration of extract of *B. monnieri* lowered the alcohol-induced increased enzymes such as γGT, ALP and LDH. The extract restored the enzymatic activities (aspartate and alanine aminotransferases, gamma-glutamyl transpeptidase and alkaline phosphatase) and total bilirubin, total protein and albumin in serum. The possible reason for hepatoprotective activity is its ability of reduction of fat metabolism and free radical scavenging activity (Singh et al., 2015).

 doi:10.20944/preprints202507.0981.v1

6.6. Cardioprotective Activity

Saponins and flavonoids present in *B. monnieri* are reported to produce vasodilation. Flavonoids present in *B. monnieri* such as luteolin and apigenin are reported as potent vasodilators but due to its high content, saponins have greater effect on vasodilation as compared to flavonoids. Combination of flavonoids and particularly the saponins, have greater clinical significance to improve blood flow and cognitive function (Kamkaew et al., 2019). Other studies demonstrated that extracts of *B. monnieri* partly reduces blood pressure via releasing nitric oxide from the endothelium and have an additional effect on vascular smooth muscle Ca^{2+} homeostasis (Kamkaew et al., 2011).

Due to its ability to recover coronary flow, contractile force and function, and reduced infarct volume, *B. monnieri* is a promising cardioprotectant (and cerebroprotectant) for patients at risk from infarcts (Srimachai et al., 2017). The blood pressure reducing activities of this ayurvedic medicinal plant is due to the presence of Bacoside A3 and bacopaside II that belongs to class jujubogenin and pseudojujubogenin respectively (Kamkaew et al., 2011). Myocardial salvaging effect of *B. monnieri* in the presence of diabetes mellitus was studied and assessed by Ghatage et al (2014). This study indicates the promising anti-diabetic with potential cardiovascular benefits of this herb.

Extracts of *B. monnieri* maintains myocardial integrity and cardiac rhythm by restoring expressions of Nrf2, HO-1, and NQO1 followed by elevating total glutathione levels and antioxidant enzymes (Mohan Manu et al., 2019). Cigarette smoke causes lipid peroxidation, which leads to cellular damage and increased membrane permeability in the heart that causes the release of creatinine kinase enzyme. It was reported that Bacoside A induces anti-lipid peroxidative effect and free radical scavenging activity that leads to improved integrity of the membrane and hence prevented leakage of creatinine kinase (Anbarasi et al., 2005).

7. Conclusion and Future Prospects

Plants are regarded as green factories due to their ability to produce natural products beneficial to mankind. Traditional and ethno-botanical evidences are the basis of dugs discovery from plants. The traditional system of Medicines claims the therapeutic use of numerous plants. Plant-based drugs are favored because they have fewer or no side effects. Extensive research has been done on this plant related to its scent, but there is brief knowledge available about its pharmacological profile. This review is an attempt to compile the information on pharmacological effects of *B. monnieri* in a comprehensive manner. The presence of various bioactive constituents with low toxicity profiles and the new mechanism of action make Brahmi an effective drug candidate for the treatment of different diseases. The diverse bioactive agents present in *B. monnieri* participate in treating various ailments of the human body. Reports suggested that *B. monnieri* is pharmacologically active as an anticancer, antifungal, antibacterial and antioxidant agent. However, extensive researches related to the Phytochemistry, pharmacology and biotechnology are needed to develop a drug from *B. monnieri*.

Since *B. monnieri* is well known as a possible source of various chemical constituents, this herb holds a prominent position among many significant medicinal plants. There exist different bioactivities of *B. monnieri*; hence more research is required to expose the underlying mechanisms of drug compound action. If the correlation of particular metabolite (chemical constituent) of *B. monnieri* were scrutinized, it would provide better opportunities for future researchers to develop a potential drug from this plant. The large-scale consumption of *B. monnieri* by humans as a remedy of healthcare in traditional systems of medicines, further screening and investigation of various formulations for different bioactivities *in-vivo* and *in-vitro* is essential.

Conflict of Interests: The authors declare that they do not have conflict of interest with anyone.

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