J. Sci. Innov. Nat. Earth: Vol. 5, Issue 3, 2025, Page 04-07 ISSN (Online) 2583-2093

OPEN ACCESS

Journal of Science Innovations and Nature of Earth

Journal homepage : https://jsiane.com/index.php/files/index

International, Double-Blind, Quarterly, Peer-Reviewed, Refereed Journal, Edited and Open Access Research Journal

The Antioxidant Activities of Secondary Metabolites in Medicinal Plants: A Comprehensive Review

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DOI: https://doi.org/10.59436/jsiane.409.2583-2093

Abstract

The antioxidant activity of medicinal plant secondary metabolites is examined in this review. Metabolic activities generate free radicals and unstable molecules; these substances, which include terpenoids, tannins, alkaloids, steroids, flavonoids, and phenolic acids, protect vital biomolecules including DNA, RNA, proteins, and lipids from harm. Oxidative stress, which includes free radicals, is associated with long-term health problems like diabetes, cancer, and heart disease. Eleutherine americana, *Ocimum sanctum*, *Syzygium cumini* , Dalchini, *Saraca indica*, Sita Ashok, and *Syzygium cumini* are some medicinal plants that are high in these antioxidants. Other examples are Baobab, Tulsi, *Adansonia digitata* , *Syzygium cumini* , *Syzygium cumini* , and Red Bulb Plant. In order to use these secondary metabolites in functional foods, nutraceuticals, and medicines, it is crucial to understand their antioxidant processes, as highlighted in the review. When compared to synthetic compounds such as butylated hydroxy toluene (BHT) and butylated hydroxy anisole (BHA), natural antioxidants are a safer bet for health promotion and illness prevention.
Keywords: Secondary metabolites, Antioxidant, Free radicals, Medicinal plants, Flavonoids.

Received 10.06.2025 Revised 15.07.2025 Accepted 20.08.2025 Online Available 03.09.2025

Introduction

Phytochemicals, also known as secondary metabolites (SM), are a class of carbonic molecules produced by plants. They aid in disease resistance and have strong antioxidant capabilities. According to Kılıç *et al*. (2017), antioxidants aid the digestive and immune systems of the human body. According to Velu *et al*. (2018), secondary metabolites have a broad range of therapeutic effects and most of them interact directly with receptors, cell membranes, and nucleic acids. Today, pharmacology faces a challenge from the diversity of SM and their methods of action, whether they are used alone or in natural mixtures found in plants (Wink, 2015). Many plant components, including leaves, roots, fruits, seeds, and more, contribute to the body's supply of phytochemicals. All parts of the plant have different medicinal properties and include secondary metabolites that may be used to make medicines and cure different diseases (Pammi *et al*., 2023).

A significant part of preventing degenerative illnesses is the presence of chemical molecules with antioxidant action, which are abundant in plants. This imbalance is a major contributor to many long-term health issues, including diabetes, cancer, heart disease, and neurological disorders like Alzheimer's and Parkinson's. According to Chanda and Dave, (2009). Decrease in heritable alterations that promote cancer progression. In order to improve health, medicinal shops contain a wide variety of secondary metabolites. This suggests they might be rich in compounds that neutralize free radicals; as such, they warrant investigation as potential antiradical agents. All humans require these chemicals in their diets (Merkl *et al*., 2010).

There are a variety of carbonic composites that plants may generate; these are known as secondary metabolites, and they can help lower levels of oxidative stress in the body. Traditional medicines have their roots in plants. As stated by Jain *et al*. (2019) in addition to well-known compounds like carotenoids, flavonoids, or polyphenols, secondary metabolic agents often display the extracts' antioxidant properties through a number of means. The reference is from Farzaneh and Carvalho (2015). In addition to being required for cellular viability, these secondary metabolites aid in cellular commerce with their environment and prevent waste products from chelating vital molecules (Pagare *et al*., 2015).

Benes *et al*. (1999) states that enzymes like catalase, glutathione peroxidase, and superoxide dismutase are crucial in neutralizing free radicals and protecting cells from damage. Cells have many defense mechanisms against reactive oxygen species (ROS) to keep redox equilibrium in check. Scavenging reactive oxygen species (ROS) is one possible mechanism of action. Matkowski, (2008) lists binding metals or blocking enzymes as other ways to prevent ROS generation. One of the many crucial aspects of aerobic metabolism and plant life is the role of phenolic composites in the cell defense system, which in turn lowers metabolic effort in the body. According to Rash, (2014), oxidative stress caused by free radicals is strongly associated with the development of the diseases. The increasing demand for herbal pharmaceuticals, natural health products, and medicinal plant secondary metabolites has led to a rapid expansion of medicinal plant usage across the world (Nalawade *et al*., 2003). New research has also shown that plants' antioxidant capabilities are mostly due to their polyphenolic components. In-vitro and In-vivo studies have shown that some plant compounds and secondary metabolites can mitigate disease-causing agents (Gupta *et al*., 2019). A contemporary medicine's basis is in the reasons of degradation of plant-based natural chemicals. One way to lessen the effects of oxidative stress is using an antioxidant. Some secondary metabolites protect the body's molecules against free radical degradation, according to research by Senguttuvan *et al*. (2014). Exogenous sources include ionising radiation, tobacco smoke, pollutants, pesticides, and chemical solvents; endogenous sources include respiration and peroxisomes stimulation of polymorphonuclear leucocytes and macrophages.

These free radicals have the ability to harm cells by oxidising DNA, lipids, proteins, and nucleic acids. Thus, these characteristics can lead to degenerative disorders (Patel *et al*., 2012). Concerns about the rising toxicity in the body from conventional therapies have led to a rise in interest in herbal medicine and the use of plant extracts as herbal medicine, alongside the development of important treatments for diseases originating in the body (Nwozo *et al*., 2023).

a)Importance of Antioxidants in Human Health-Recently, medicinal plants have gained popularity as a potential alternative or supplement to conventional medicine (Kawamura & Muraoka, 2018). Medicinal plants are used by many for the treatment and cure of sickness due to their soothing characteristics and lack of harmful consequences. Ernst (1998) reports. Herbal remedies derived from plants are gaining popularity as a means of illness prevention in the modern world. Herbal remedies are a great alternative to manufactured pharmaceuticals since they are safer, more accessible, and less expensive.

A variety of biologically active carbonic molecules known as secondary metabolites are biosynthesized from primary metabolites. Reducing oxidative stress and protecting vital components from degradation are two of their functions (Jain *et al*., 2019). Many diseases and health problems can be brought on by oxidative stress, as stated by Marcetic and Arsenijevic, (2023). By both stimulating natural antioxidant processes and neutralizing free radicals produced in the body's cells, secondary metabolites can have an antioxidant role. Due to their extreme reactivity and the existence of unpaired electrons, free radicals are also known as unstable molecules. In an effort to maintain their stability, they take electrons from neighboring molecules, which can lead to oxidative damage to DNA, lipids, and proteins. Both internal and environmental factors, including pollution, radiation, and poor dietary choices, contribute to the formation of free radicals.

Role of Medicinal Plants as Natural Sources of Antioxidants- According to Williams *et al*. (2004), medicinal plants are the primary source of antioxidants. The scavenging activity of free radicals was tested using DPPH, which stands for 1,1-diphenyl-2-picrylhydrazyl (Khalaf *et al*., 2008).

These radicals can be scavenged by both natural and synthetic antioxidants. Meanwhile, it has come to light that several synthetic antioxidants, such BHT and BHA, are detrimental to human health if consumed in large quantities. A lot of individuals are interested in adopting natural antioxidants instead of synthetic ones as they are believed to be safer (Mbaebie *et al*., 2012). One potential benefit of secondary metabolites is their ability to lower the risk of illnesses including cancer, heart disease, and stroke by increasing plasma's antioxidant capacity. Some of the secondary metabolites present in plants, such flavonoids and phenolics, have the ability to scavenge free radicals. You can find them in just about every plant component, including the fruit, leaf, seed, bark, root, and stem (Mathew & Abraham., 2006).

b)Scope of the Review- The antioxidant capabilities of medicinal plant secondary metabolites are the subject of this review. It delves into the impact of oxidative stress in disease development and compares synthetic antioxidants to their natural counterparts. Secondary metabolites including alkaloids, tannins, terpenoids, flavonoids, and saponins are studied, along with their antioxidant mechanisms and methods of manufacture. Among these processes are the regulation of antioxidant enzymes, metal chelation, and free radical scavenging.

c)Secondary Metabolites in Medicinal Plants

•Definition and classification of secondary metabolites

Secondary metabolites are organic chemicals that plants make; they aren't required for basic metabolic processes, growth, or reproduction. But they play a key role in ecological interactions, signaling, and defense (Bourgaud *et al*., 2019), particularly in the face of oxidative stress, herbivores, and infections. Generally speaking, secondary metabolites may be categorized into three types based on their metabolic source:

(i) Terpenoids (isoprenoids), which are produced by the mevalonate and methylerythritol phosphate (MEP) pathways and include monoterpenes, diterpenes, triterpenes, carotenoids, and steroids, and which are known for their functions in defense, pigmentation, and aroma.

(ii) Phenolic compounds, which are derived from the shikimate and phenylpropanoid pathways and include flavonoids, tannins, lignins, and phenolic acids.

(iii) Compounds that contain nitrogen and Sulphur, such as alkaloids, glucosinolates, and cyanogenic glycosides, many of which have strong pharmacological activities (Yang *et al*., 2018; Singh & Sharma, 2022).

•Major Classes of Antioxidant Secondary Metabolites

There is an abundance of the following secondary metabolites in medicinal plants; they are part of a larger class of carbonic compounds that find extensive application in the pharmaceutical and medicine industries.

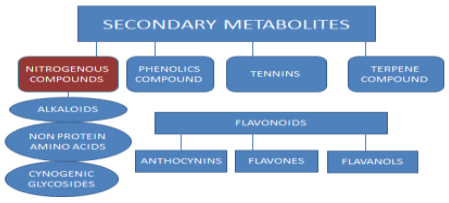

Figure1. Shows types of secondary metabolites

S.No.	Types of Secondary Metabolites	Properties	Refrences
1.	Terpenes (Terpenoids and Steroids)	Terpenes have a significant role as secondary metabolites. These compounds, which include aromas of flowers, all include five-caron isoprene units that repeat.	(Croteau *et al.*, 2000)
2.	Coumarins and stibenes.	Coumarins, a large class of plant metabolites, are present in the greatest concentrations. What we term benzopyrone is actually a benzene ring fused to α-pyrone.	(Tiwari & Rana 2015).
3.	Alkaloids	Plant alkaloids are chemicals with an amine functional group—a heterocyclic ring that contains one or more nitrogen atoms.	(Roaa, 2020).
4.	Phenols	The phenolic class of secondary metabolites is the most extensive. The chemicals might be as simple as a single aromatic ring or as complex as polymers like tannins and lignins.	(Da Silveira *et al.*, 2020)
5.	Flavonoids	These are aromatic compounds. This means that in their chemical structure, instead of a straight or branched chain, a cyclic carbon (aromatic) ring is present.	(Mohiuddin, 2019)

d) Mechanisms of Antioxidant Action:

Free radicals and oxidative stress-According to research conducted by Lobo *et al*. (2019), free radicals are incredibly unstable molecules or atoms with the ability to initiate chain reactions due to their one or more unpaired electrons. The most common free radicals in biological systems are reactive nitrogen species (RNS), such as nitric oxide (NO) and peroxynitrite ($ONOO^{\cdot}$), and reactive oxygen species (ROS), such as superoxide anion ($O_2^{\cdot}$), hydroxyl radical (OH-), and peroxyl radicals.

Damage to macromolecules such as proteins, DNA, and lipids can occur as a result of oxidative stress when the production of free radicals outstrips the capacity of the body's antioxidant defenses. The imbalance has been associated with a wide range of degenerative and chronic illnesses, including cancer, diabetes, atherosclerosis, neurological problems, and ageing (Pham-Huy *et al*., 2008; Yadav *et al*., 2021).

Antioxidant defense systems-

1.Enzymatic antioxidant:- According to (Gill & Tuteja 2010), by transforming superoxide and hydrogen peroxide into water and oxygen, enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT), ascorbate peroxidase (APX), and glutathione peroxidase (GPx) help medicinal plants detoxify ROS (reactive oxygen species) and preserve cellular redox equilibrium.

2.Non-enzymatic antioxidant:-Ascorbic acid, tocopherols, carotenoids, glutathione, phenolics, and flavonoids are examples of non-enzymatic antioxidants that function as membrane stabilizers, metal chelators, and radical scavengers, protecting plant cells and adding to their therapeutic value (Foyer & Noctor, 2011).

e) Antioxidant Properties of Selected Medicinal Plants:

1. Red bulb plant or also called "bawang dayak" (Eleutherine americana Merr)- Kuntorini and Astuti, 2010 found a molecule in red Banjarbaru bulbs that can prevent cell damage. At a concentration of 25.33 parts per possible, the material is known as ethanol extract and it is effective. The chemical components of the red bulbs, including quinones and triterpenoids, were also examined in the study. They lessen oxidative stress and have antioxidant characteristics. The bulbs of this plant include quinones, triterpenoids, and naphthoquinone groups (e.g., eleutherine, elutherole, and eleutherinone) (Kuntorini *et al*., 2016). The cytoprotective and anti-aging effects of this chemical are enhanced by antioxidants, and it may help reduce oxidative stress associated with chronic diseases such as diabetes, hypertension, and heart disease.

Figure 2: (*Eleutherine americana Merr*) or Red bulb plant

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2. Ocimum species or Tulsi- There is a significant significance for the chemical components of plants that have antioxidant qualities in preventing a variety of degenerative disorders in the body (Velioglu *et al*., 1998). Research has shown that the antioxidant properties of herbs and spices are strongly correlated with the concentration of phenolic compounds, which are redox agents that may operate as hydrogen donors, quenchers of singlet oxygen, and reducing agents (Caragay., 1992). Common to many plants in the Lamiaceae family, the plant's primary constituents are phenolic chemicals, a type of secondary metabolite. The antioxidant capabilities of *Ocimum sanctum* are the highest of all of the Ocimum species investigated (Hakkim *et al*., 2007). Metabolite content of *Ocimum sanctum* has been described lately, with compounds having antioxidant action; this is an important step in identifying secondary metabolites in Ocimum species. The plant contains phenolic compounds, flavonoids, coumarins, tannins, phenylpropanoids, and terpenoids (Mandal, *et al*., 2022). There have been reports of several pharmacological actions, including antibacterial, free radical scavenging, anti-stress, and antioxidant properties.

Figure 3: *Ocimum sanctum* or Holy Basil

3.*Adansonia digitata* L. or Baobab plant:-Ibrahima *et al*. (2014) states that although the baobab tree (*Adansonia digitata*) in Africa has been the subject

of several research, the antioxidant activity of various fruit portions and the presence of secondary metabolites have received relatively less attention. Several studies have looked at the anti-inflammatory and antioxidant properties of baobab. The antioxidant activities of methanolic extracts of various baobab fruit sections are enhanced by the presence of polyphenols, flavonoids, and tannins, as described by Ndiaye *et al*. (2021). Additional phytochemical analysis of the fruit extracts showed that they included tannins, saponosides, sterols, alkaloids, coumarins, flavonoids, and total sugars. Research has revealed that procyanidins and flavanol glycosides are plentiful in tiliroside, the primary component of baobab fruit pulps. The profile of baobab leaves was comparable to that of fruits, except there were more phenolics identified in the leaves. According to Braca *et al*. 2018 polyphenols, have a high scavenging capacity, and the pulp extract has strong reducing power, which means it may give electrons.

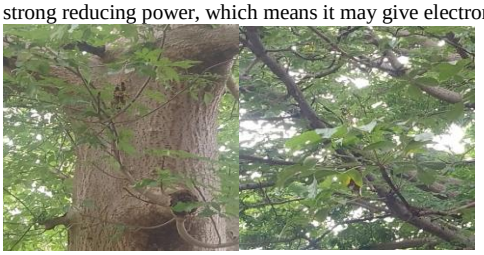

Figure 4: (*Adansonia digitata L.*) Baobab Fruit

4. *Syzygium cumini* or blackberry- Recent research has linked *Syzygium cumini L.* to the antioxidant-rich Myrtaceae family, which includes the popular Jamun and blackberry fruits. Primarily, this plant grows in India. In addition to this, it may also be found in the Americas, some parts of Asia, and nations in eastern North America. The plant produces fruits that are pink in colour with pulp that is deep purple or blue. They have several medicinal uses, such as an antidiabetic and an anti-chronic diarrhoea agent, in addition to their fruit consumption and high antioxidant content. There is evidence that blackberry fruits have powerful antioxidant capabilities in addition to their antidiabetic effects. Using acidic ethanol, the anthocyanins and other polyphenols were removed. According to the data, there were 0.54 anthocyanins, 0.17 ellagic acid, and 1.15 polyphenolics in the pulp cream. Although they possessed a high concentration of ellagic acid, blackberry seeds did not contain any practical anthocyanins (Aqil *et al*., 2012).

It is a food and medicine treasure trove because of the bioactive compounds found in its leaves, bark, fruits, stems, and roots, which include ellagic acid and other flavonoids, phenols, lipids, and alkaloids (Arya *et al*., 2019). The phenolic compounds found in fruits are powerful antioxidants and anti-diabetic agents.

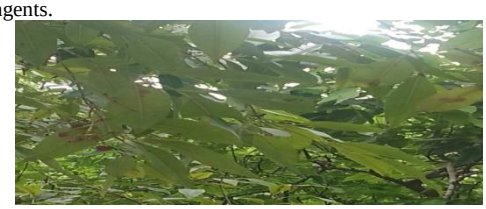

Figure 5: *Syzygium cumini* or blackberry

5. *Syzygium cumini* Roxb or Sheesham- *Syzygium cumini* is a kind of hardwood tree native to India (Roy *et al*., 2011). It goes by other names than just "rose" in India; the Sheesham is another one. The multi-colored bark of this tree has a wide variety of therapeutic uses in traditional Indian medicine. Because flavonoids have powerful antioxidant effects, this factory's flavonoid composites have been the subject of much research into their potential for vibrant natural conditioning in the body. Among these compounds are a recognised flavone, a novel chalcone, and an isoflavone (7- , 5-hydroxy-4'-methoxyisoflavone). *Syzygium cumini* 's root bark yielded 7-hydroxy-6-methoxyflavone, biochanin A, and dehydrohemomorphigenin, three recognised rotenoid compounds. The methanolic extract of *Syzygium cumini* yielded a variety of compounds, including two novel forms of open-chain neoflavanoids and a blend of additional chemicals having flavonoid properties. According to Bajpai (2023), *Syzygium cumini* has a wealth of chemicals, including flavonoids, tannins, alkaloids, phytosterol terpenoids, coumarins, and phenolic compounds.

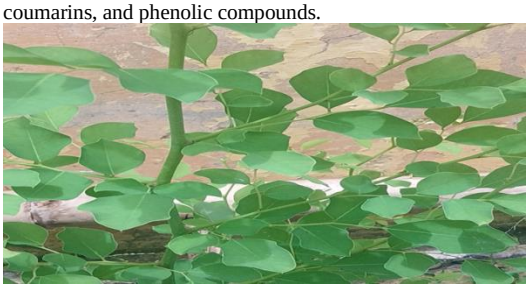

Figure 8: *Syzygium cumini* Roxb or Sheesham

Its leaves bark, and heartwood extracts have been shown to increase the antioxidant defense of cells by using phenolic and flavonoid chemicals. These characteristics imply that *Syzygium cumini* might be used therapeutically to combat oxidative stress.

6. *Syzygium cumini* or Dalchini:-The plant's antioxidant effect is attributed to bioflavonoids, which are found in *Syzygium cumini* , also known as dalchini (Katiyar *et al*., 2013). Their chemical components and medical uses are the main points, and they also have antioxidant capabilities.

Figure 6: *Syzygium cumini* or dalchini

Their long history of usage in herbal therapy is due to the powerful antioxidants they contain. It is believed by many scientists that around two-thirds of all plant species possess some kind of therapeutic value. The presence of bioactive chemicals, such as flavonoids and polyphenols, gives many of them great antioxidant potential.

7. *Saraca indica*, commonly or Sita- Ashoka:- Phytochemicals, such as flavonoids, are derived from floral and leaf sources. In addition to β-sitosterol glucoside, three flavonoids -epicatechin, epiafzelechin-(4β→8)-epicatechin, and procyanidin B2 were extracted from the dried bark. Plant bark includes epicatechin, catechin, procyanidin p2, 11'-deoxyprocyanidin B, and other compounds. *Saraca indica* bark extracts (ethanolic, hydroalcoholic, and acetone) have been found to have antioxidant activity in many publications.

Figure 7: *Saraca indica* of Ashok tree

According to reports, these bioactive chemicals are responsible for the antioxidant, anti-inflammatory, and cytoprotective effects of ethanolic, hydroalcoholic, and acetone extracts of flowers, leaves, and bark. In hormone-dependent tissues, it regulates oxidative stress and prevents cancer-causing oxidative DNA damage. Additionally, it scavenges free radicals like O_2-and OH-.

Conclusion

Antioxidant characteristics of medicinal plant secondary metabolites serve to halt the effects of free radicals, which are unstable molecules produced by metabolic processes in the body. This is a powerful tool in the fight against cancer, heart disease, and diabetes since it lowers the body's oxidative stress levels. To eliminate oxidative stress and neutralize free radicals, substances like tannins, alkaloids, phenolic compounds, etc., employ biological chemical processes. The increasing popularity of plant-based antioxidants raises the possibility that these compounds are superior to their synthetic counterparts in terms of efficacy, safety, and overall usefulness. This quality improves immunity and safeguards the cardiovascular system and brain. When it comes to protecting cells from oxidative stress, it's a major player in disease prevention. Medicinal plant secondary metabolites are rich with untapped potential for application in functional foods, nutraceuticals, and pharmaceuticals. To sum up, these substances are incredibly useful for controlling reactive oxygen species (ROS), eliminating free radicals, bolstering treatments that rely on antioxidants, and generally improving people's health.

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