The Presence of Bioactive Compounds in Plants of the Amaranthaceae Family and Their Use in Medicine: A Review

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Literature review

Abstract: *Various plants have been used in traditional medicine for thousands of years as natural medicines with therapeutic and other pharmacologic effects. Bioactive compounds found in plants, such as flavonoids, trace minerals, essential oils, phenols, glycosides, alkaloids, and tannins, can affect microbial growth, reproduction, and essential cell functions. Plants of the Amaranthaceae family have a broad range of bioactive phytochemical constituents, which provide a variety of medicinal benefits. This review article discusses the characteristics of Amaranthaceae plants that may indicate their use as medicinal plants, especially against infectious diseases. According to the literature, Amaranthaceae plants contain considerable levels of bioactive compounds that make them effective in traditional medicine, even* though their impact on numerous microbes has yet to be examined.

Keywords: Active compounds, Amaranthaceae, antioxidant, antibacterial, flavonoids.

1. Introduction

Since ancient times, different plants are utilized in traditional medicine as natural medicines with therapeutic and other pharmacologic effects. According to the World Health Organization (WHO), traditional medicine is used by up to 80% of the world population for main healthcare needs. The first findings of a WHO study reveal that the number of people who use medicinal herbs is considerable and growing, even among the young population. In addition, the World Health Organization recommends medicinal plants as the best source of a wide range of drugs [1, 2]. Plants or some of their parts, such as leaves, roots, seeds, and flowers, can be used in a variety of ways, including fresh crude form and teas, decoctions, powder form, or extracted forms [2].

2. Bioactive Compounds

Plants contain active components that may impact the growth of microorganisms, reproduction, or some essential cell activities. Some examples of active compounds include phenols, flavonoids, trace minerals, essential oils, glycosides, alkaloids, and tannins, which could be used in the production of drugs. The extracts of medicinal plants are also utilized as preservatives in food, preventing harmful microorganisms from growing [2, 3]. Flavonoids and phenolic compounds are characterized as an effective antioxidants, anticancer, antimicrobial agents, anti-inflammation, immunological response boosting agents, skin protection agents, and potential pharmaceutical and medical agents. Due to numerous advantages for human health, research dealing with flavonoids and other phenolic compounds from medicinal plant species has increased significantly over time [4]. Plants and their bioactive components play a significant role in the search for new antimicrobial agents. Specific phytomolecules have been shown to block bacteria's quorum-sensing function, suggesting that they could be utilized to treat infections associated with bacterial biofilms [5]. Aside from medical uses, medicinal plants may be beneficial to human nutrition because they also contain various bioactive chemicals such as vitamins and essential oil components. Because of the presence of antioxidants and antibacterial elements, as well as the flavoring and coloring qualities of several medicinal plants, they are usually utilized in food products and cosmetics [2].

3. Amaranthaceae Family

There are more than 165 genera and 2040 flowering plant species in the Amaranthaceae family, which can be found all over the world, from tropical to cold temperate areas [6]. Within the flowering plant order Caryophyllales, it is the most species-rich lineage. The Amaranthaceae family includes annual and perennial species, predominantly herbs, as well as bushes, tiny trees, and grapevines. Several species were used as medicinal plants by natives in tropical and subtropical regions, as well as in temperate climates, for a variety of purposes [7]. Research has revealed that Amaranthaceae extracts have antioxidant [8, 9], antidiabetic [10, 11], immunostimulatory, antitumor, antimicrobial, analgesic [12], anti-inflammatory [13], hypolipidemic [14], diuretic [15], antihypertensive, and hypoglycemia [16] properties. Also, they contain biologically active substances such as betacyanins, flavonoid compounds, phenols, volatile oils, diterpenes, etc. [7, 17, 18]. The most prominent genera and species from the Amaranthaceae family are amaranth (*Amaranthus*), smotherweed (*Bassia)*, chard (*Beta vulgaris*), cockscomb (*Celosia)*, glasswort (*Salicornia*), globe amaranth (*Gomphrena globosa*), goosefoot (*Chenopodium*), orache (*Atriplex*) and spinach (*Spinacia oleracea*) [18, 19].

Amaranth (Amaranthus)

Amaranthus, often known as Green Amaranth, is described in Greek as "never fading." Most plants in the genus are usually thought of as weeds, however, others are grown as leafy vegetables in various regions of the Earth, while phytonutrients that participate in the reduction of free radicals have been observed in various parts of plants [20]. Phytochemical investigations of these vegetables have shown the presence of phytochemicals involved in radical scavenging activities, such as flavonoid compounds, alkaloid compounds, tannins, phenols, glucosides, and glycosides [21, 22]. *Amaranthus* is characterized as an antioxidant, antibacterial, anti-inflammatory, antimalarial, antidiabetic, anticancer, and hepatoprotective agent [23, 24].

Stintzing et al. (2004) used quantitative and qualitative analyses of phenolic compounds and betalains from stem extracts to confirm the antioxidant properties of *Amaranthus spinosus* L. The major betacyanins detected in *A. Spinosus* L. were amaranthine and isoamarantine, and hexacinamates, quercetin, and kaempferol glycosides [25]. Kraujalis et al. (2013) also investigated the antioxidant characteristics of solid plant material and discovered that amaranth leaves and flowers, as well as their extracts, have high antioxidant activity [26]. El-Shabasy & El-Gayar (2019) compared six species of the Amaranthaceae family (*Aerva javanica, Aerva lanata, Amaranthus graecizans* ssp. *silvestris, Amaranthus hybridus* L., *Amaranthus viridis* L., and *Digera muricata* L.) based on their antimicrobial properties and concluded that they have an antimicrobial effect against some pathogenic bacteria [27].

Smotherweed (Bassia)

Bassia is an annual plant genus in the Amaranthaceae family containing about ten species native to Eurasia. Many *Bassia* species can survive in saline soil and are toxic to grazing animals, especially sheep. The five-horn smotherweed (*Bassia hyssopifolia*) and hairy smotherweed (*Bassia hirsuta*), both brought to the Americas, are considered invasive in locations outside of their native habitat [28]. The genus' members are generally plants or subshrubs with dense hairs covering them. The slender leaves are sessile (meaning they don't have a leafstalk) and alternate along the stems. The bisexual blooms are produced in terminal spikes with unique hooked or conical appendages. Achenes with little brown seeds are the fruits [28, 29]. The chemical content of *Bassia* extracts was primarily studied for pharmacological investigations, to detect biological activities and develop new pharmaceuticals. According to traditional medicine, plants of this genus exhibit antiparasitic, cardioprotective, tonic and other properties [30]. Scientific and clinical studies examining hypotensive, hypolipidemic, anticarcinogenic, analgesic, and other effects [31, 32, 33], have shown the presence of flavonoids, tannins, saponins, and alkaloids for the species *B. prostrata, B. scoparia*, and *B. muricata* [34–37].

The presence of eleven phenolic compounds in *Bassia prostrata* plants was investigated and confirmed by Petruk et al. (2021), and the quantitative amount of each chemical ranged from 0.1 to 10.8 mg/g [30]. Al-Snafi (2018) stated that the fruit of Kochia scoparia (*Bassia scoparia*) was used in China to treat skin, urinary tract, and eye disorders, as well as in Japan as a meal. It was also commonly used in Southeast Asia to treat painful urination, skin issues, breast pain, and malignancies, as well as a food supplement and treatment for inflammatory conditions like arthritis and chronic pain. Kochia scoparia was applied in traditional Korean remedies as a tonic, diuretic, analgesic, and antidote [34]. Significant amounts of flavonoids and saponins in aerial parts of *B. muricata* were isolated in a study done by Kamel et al. (2001) [35]. Also, Shaker et al. (2013) have demonstrated the presence of flavonoids and saponins in *B. muricata* and proven the antioxidant power of this plant [36].

Chard (Beta vulgaris)

Beta vulgaris L. is native to southern and eastern Europe as well as northern Africa. It can be found in Europe, Asia, America, and Africa. Because it contains a variety of nutrients and biologically active compounds, as well as high levels of antioxidants, vitamins, and other components with health-promoting effects, *B. vulgaris* is very often used in diet [38]. The leaves of chard (*Beta vulgaris* L. subsp. *vulgaris*) contains high levels of vitamins A, B, and C, as well as calcium, iron, and phosphorus. *B. vulgaris* species are also used in traditional medicine for liver and kidney problems, immunological and hematopoietic system activation, and as a special diet in cancer treatment. They also lower blood pressure and improve endothelial function [38, 39]. Chard leaves are rich in phytochemicals and antioxidants such as flavonoids, phenolic acids, pigments, and certain volatile compounds like anethole, which has an antibacterial and antifungal impact [40].

Pyo et al. (2004) were the first to show that the methanol extract of chard contains both phenolic acids and flavonoids as antioxidant components. They concluded that the antioxidant activity of each chard extract may be connected to their phenolic concentration [41]. Sacan and Yanardag (2010) investigated the antioxidant capabilities, acetylcholinesterase inhibitory capacity, and proline content of chard. Their findings were compared to natural and manufactured antioxidants, showing that chard could be a natural source of antioxidants, antiacetylcholinesterase, and proline [39]. Mzoughi et al. (2019) looked at the chemical properties of chard leaves as well. The findings of this study emphasized the wild Swiss Chard's potential medical advantages as a source of dietary and biologically active components [40].

Cockscomb (Celosia)

The name *Celosia* comes from the Greek word *kelos*, which means "burned," and describes flower heads that resemble flames. If the blooms are crowned with fasciation, they are known as wool-flowers, brain celosia, or cockscombs. The *Celosia* species are used in traditional medicine to treat a variety of conditions, including fever, diarrhea, mouth ulcers, irritation, injuries, and infections [42, 43]. Triterpenoids, saponins, betalains, alkaloids, phenolic compounds, tannins, flavonoids, glycosides, sterols, etc., are among the phytochemical compounds isolated from *Celosia* species [44–48] and they contribute to antiinflammatory, immunostimulatory, anticarcinogenic, hepatoprotective, antioxidant, tissue repair, hypoglycemic, antinociceptive and antimicrobial activity [47–50].

Celosia is a genus of roughly 60 species endemic to subtropical and temperate regions of Africa, South America, and Southeast Asia. *C. argentea* seeds are used in Chinese herbal medicine to treat ocular and liver problems. Also, dried mature seeds are used to cure diseases including hepatitis, hypertension, and sarcoptidosis, as well as to enhance vision [51]. In the research conducted by Hakawa et al. (1998), the anticarcinogenic effect of *C. argentea* seed extract was confirmed. It is dependent on immunomodulation features such as cytokine induction, which resulted in a Th1 dominant immune state, stimulating macrophages to a tumoricidal state, preventing cancer spread [52]. It is also reported that

C. argentea contains flavonoids, which have antiproliferative properties against a variety of human cancer cells [53, 54]. Rub et al. (2016) analyzed the phytochemical composition of *C. argentea* and found flavonoid and phenolic compounds, both of which are effective scavengers of reactive oxygen species, and whose activity might be used to support the anticancer and antioxidant potential of this plant [55].

Glasswort (Salicornia)

In Europe, the genus *Salicornia*, particularly the tetraploid species, is often used as a vegetable. The seeds are high in oil, and various trials have been conducted in the United States to commercialize tetraploid species, particularly *S. bigelovii*, as a source of vegetable oils [56]. Some *Salicornia* species are used in the diet [57], as well as in the treatment of respiratory problems, arthritis [58], stroke, cirrhosis [59], and diarrhea [60], and have biological activities including antioxidant, anti-inflammatory, antidiabetic, and cytotoxicity [61, 62, 63]. Some of the bioactive compounds found in plants of this genus are fatty acids, sterols, saponins, flavonoids, and phenols [64–68].

S. ramosissima is an annual plant widely distributed in Portugal, France, and Serbia, and according to Isca et al. (2014), it contains a variety of phytochemicals (sterols, mono and polyunsaturated fatty acids, dicarboxylic acids, and alcohols) that are within the safe limits set by numerous international organizations [69]. Proteins, fibers, minerals, and polyunsaturated fatty acids are all found in *S. ramosissima* [70], so it is often used for the production of food supplements and in nutrition [69]. Phenolic substances including quercetin3-O-glucoside and caffeoylquinic acids have also been discovered in this plant, and they are known to help prevent diseases like cancer, hypertension, and cardiovascular disease [70]. Furthermore, the study of Ferreira et al. (2018) supports plant usage for medicinal purposes. They conducted toxicological tests on *S. ramosissima* on mice testis and concluded that it had the therapeutic potential for the male reproductive system, owing to the antioxidant activity of its ingredients [71]. Surget et al. (2014) found that *S. ramosissima* is rich in phenols and flavonoids, indicating that it has antioxidant properties as well as a UV photoprotective impact [72].

Globe Amaranth (Gomphrena globosa)

Globe amaranth, or *Gomphrena globosa*, is an annual branching plant that is grown as an ornamental flowering herb in the garden. It grows well in Bangladesh and is endemic to America and Asia [73]. Its leaves and blossoms have been used in folk medicine to treat high blood pressure, diabetes, renal and respiratory issues, and diseases of the reproductive organs [74, 75]. Biological activities were observed for extracts of various *Gomphrena* species such as antioxidant, antifungal, larvicidal, antibacterial, anticancer, and estrogenic activities [73, 76–78]. Phytochemical investigations revealed the presence of saponins, alkaloids, betacyanins, hydroxycinamamides, and flavonoids, including flavones and flavonols [78, 79, 80].

Pomilio et al. (1992) analyzed extracts and components of *Gomphrena martiana* and *Gomphrena boliviana* against Gram-positive bacteria (*Staphylococcus aureus, Streptococcus faecalis, Micrococcus luteus* and *Bacillus subtilis*), Gram-negative bacteria (*Salmonella newport, Salmonella oranienburg, Escherichia coli* B, *Escherichia coli* K 12, *Klebsiella pneumoniae, Serratia marcescens, Pseudomonas aeruginosa and Proteus vulgaris*), spore-forming Gram-positive bacteria (*Clostridium tetanii, Clostridium sporogenes* and *Clostridium butyricum*, an acid-fast bacterium (*Mycobacterium phlei*), a fungus (*Aspergillus niger*), and two yeasts (*Saccharomyces cerevisiae and Candida albicans)*. According to the findings of this research, these plants may potentially be applied in traditional medicine against some infectious agents [78]. Bioactive substances such as saponins, amino acids, nonreducing sugars, flavonoids, etc., were isolated from the methanolic extract of *G. celosioides* by Dosumu et al. (2010). The biological activities of *G. celosioides* extracts were evaluated on a variety of microorganisms; *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli*, and *Salmonella typhi* were all inhibited by the ethyl acetate and methanol extracts of the plant, while the methanolic extract was effective against *Candida albicans, Aspergillus niger*, and *Trichophyton species*. The findings of this study backed up the traditional use of *Gomphrena celosioides* to cure infectious disorders [81].

Goosefoot (Chenopodium)

Although most *Chenopodium* species are colonial annuals, the genus *Chenopodium* contains over 250 species that include herbaceous, suffrutescent, and arborescent perennials. Because of their high protein content and well-balanced amino-acid range, they have been used for ages as leafy vegetables as well as a significant grain crop for human and animal use [82]. Polysaccharides, amines and amides, phenols, flavonoids, saponins, sterols, essential oils, and other biologically active compounds [83–86] isolated from *Chenopodium* species are responsible for a variety of pharmacological properties, including antibacterial, antifungal, anthelmintic, antioxidant, antihepatotoxic, neuroprotective, anti-inflammatory, sedative, and more [87–89].

Sood et al. (2012) studied *C. album* leaves and discovered that they contain phenolic compounds that function as anti-nutrients by binding minerals, but they also have antioxidant properties. The presence of flavonoids and alkaloids in the leaves was also discovered and they have antioxidant properties as well [82]. *C. ambrosioides*, on the other hand, is used to treat injuries, pulmonary issues, inflammation, bronchitis, tuberculosis, and rheumatic diseases [90]. TrivellatoGrassi et al. (2013) studied the antiinflammatory, nociperception, and wound-healing characteristics of ethanolic extracts of this specimen's leaves and stems, and their findings supported the use of this plant as an anti-inflammatory, pain, and wound-healing treatment [91]. *C. botrys* is also a good example of a medicinal plant from the *Chenopodium* genus. Although *C. botrys* is widely used in folk medicine, most of its medical applications and therapeutic properties are not supported by scientific evidence. Flavonoids, alkaloids, and numerous terpenoids found in the herb [92] have antiparasitic, antifungal, sedative, and analgesic qualities [93]. *C. botrys* bioactive components also demonstrated efficacy against multiple tumor cells, implying that it could be a promising new potential plant for treating cancer [94, 95], though more research is needed to validate this.

Orache (Atriplex)

Atriplex L. species, often known as garden orache, red orache, or simply orache, belongs to the Amaranthaceae family. They are available in Canada, the United States, Australia, and New Zealand, as well as throughout Europe [96]. The genus *Atriplex* L. has over 270 species, many of which are used as antifungal, antidiabetic, and respiratory diseases treatments. This genus includes *Atriplex hortensis*, a halophyte that is used in food products, for treating disease in humans, and for beekeeping [97]. In traditional medicine, aerial parts are often used to treat pulmonary, gastrointestinal, and urinary disorders [98, 99]. The leaves of *Atriplex hortensis* are the most valued portion of the plant, which is regarded to be one of the earliest cultivated plants. Also, this plant is high in vitamins and biologically active compounds [100]. According to literature, bioactive compounds including tannins, phenols, alkaloids, flavonoids, and saponins were found in *Atriplex* species [101, 102].

Bylka et al. (2001) were the first scientists to isolate flavonoid sulfates from leaves of *A. hortensis* and confirmed their presence [103]. According to the literature, flavonoid sulfates have shown many pharmacological properties, such as anticoagulant, anti- inflammatory, and anticancer [104, 105, 106]. Also, Tran et al. (2022) confirmed the presence of flavonoid glycosides in *A. hortensis* var. *rubra* (red orache) [107] which are the essential phytochemicals in our diets. The antioxidant, anticancer and antitumor, hepatoprotective, anti-inflammatory, anti-diabetes, antiviral, antibacterial, and antifungal activity were all demonstrated in flavonoid glycosides [108, 109]. In addition to flavonoids, the presence of phenolic compounds (e.g. phenolic acids) in *A. hortensis* has been confirmed [96, 98]. Phenolic acids in plants play a variety of roles such as nutrient absorption, protein synthesis, enzyme activity, photosynthesis, structural components, and allelopathy [110]. They exhibit antibacterial and antiviral properties, as well as significant antioxidant effects due to the action of the hydroxyl group on their aromatic rings, and as a result, they prevent lipids and other molecules from oxidizing [111].

Spinach (Spinacia oleracea)

The plant *Spinacia oleracea* L. is usually referred to as "spinach." It is a 30–60 cm tall herb that is grown as a leafy vegetable all over the world. Some portions of spinach have been utilized in folk medicine to treat a variety of ailments [112]. It contains significant amounts of vitamins, minerals, proteins, omega-3 fatty acids [113] and many bioactive compounds which have been proven to have antioxidant, antiinflammatory, antimutagenic, antitumor, and chemopreventive properties [113, 114, 115].

Adapa et al. (2018) analyzed and confirmed the antimicrobial activity against *Streptococcus mutans* and *Lactobacillus acidophilus* strains of aqueous and ethanolic spinach extracts [112]. In research done by Iqbal et al. (2012), the antibacterial properties of *Spinacia oleracea* extracts were tested against nine mammalian pathogens: *Staphylococcus aureus, Salmonella typhimurium, Escherichia coli, Pasteurella multocida, Lactobacillus bulgaricus, Micrococcus luteus, Klebsiella pneumonia, Proteous vulgaris,* and *Staphylococcus epidermidis*. Except for *S. typhimurium* and *M. luteus*, all pathogens tested were inhibited by the aqueous spinach extracts. All of the bacterial strains examined were considerably inhibited by the ethanolic extracts, although the n- hexane extracts were particularly efficient against *S. typhimurium* and *S. aureus*. In comparison to other pathogens, sonicated n-hexane extracts exclusively suppressed *S. typhimurium* growth. According to this research, spinach could be a source of novel antibacterial agents [116]. Phenolic and flavonoid contents, as well as antioxidant activity, are confirmed in the study done by Atanassova et al. (2018). Proteins, lipids, insoluble dietary fibers, carbohydrates, and sugar levels were also evaluated, and the results suggest that spinach may offer considerable health benefits and help to prevent chronic diseases [96]. Altemimi et al. (2017) noted that spinach is also rich in defensins that exhibit antimicrobial activities. Defensins in spinach leaves are active against fungi, as well as Gram-positive and Gram-negative bacteria. The goal of this study was to recover antimicrobial compounds from spinach leaves and determine the antimicrobial effect against *Escherichia coli* and *Staphylococcus aureus*. They concluded that spinach leaf extracts have bactericidal properties by triggering DNA mutations in bacteria and disrupting their cell walls [117].

4. Conclusion

Medicinal plants have been used in folk medicine for thousands of years, and numerous scientific studies have confirmed their effects. The key to their application lies in the presence of various bioactive substances such as phenols, flavonoids, trace minerals, essential oils, glycosides, alkaloids, tannins, etc., the content of which has been proven in the Amaranthaceae family of plants.

This paper presents an overview of 9 plants (*Amaranthus, Bassia, Beta vulgaris, Celosia, Salicornia, Gomphrena globosa, Chenopodium, Atriplex*, and *Spinacia oleracea*) from the Amaranthaceae family. Each of them has shown to have a high proportion of bioactive substances, thanks to which they are applicable in the treatment of various diseases or for the preparation of pharmacological products.

Most of these plants, such as *Bassia, Beta vulgaris, Salicornia, Chenopodium, Atriplex*, and *Spinacia oleracea,* are used in the diet because of their high-nutrient ingredients. Also, all of the mentioned plants have antioxidant activity, while only *Amaranthus, Beta vulgaris, Celosia, Chenopodium, Atriplex*, and *Spinacia oleracea* have been shown to have antibacterial activity. Interestingly, anticancer effects of certain species, such as *Amaranthus, Bassia, Beta vulgaris, Celosia, Salicornia,* and *Atriplex*, have also been mentioned in the literature, but more research is needed to prove their effectiveness. Other applications of these herbs in medicine are mainly related to the prevention of skin diseases, respiratory tract diseases, urinary tract diseases, liver diseases, high blood pressure, diarrhea, diabetes, and cardiovascular diseases.

Since Amaranthaceae plants have been successfully tested for various biological activities, and some of their parts have been identified with a high content of biologically active compounds, it can be concluded that these plants are very important in medicine. Most studies have been performed to confirm their antioxidant, anticancer, and anti- inflammatory effects, while only a few studies have tested the antimicrobial activity of these species. Due to the growing number of infectious diseases, it would be good to do tests of different plant species on different types of infectious agents. Also, more research is needed on the direct effect of bioactive substances on diseases of organs such as lungs, stomach, skin, reproductive organs, etc.

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