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REVIEW PAPER

Bioactive Substances from Natural Sources: From Human Health to Sustainable Agriculture

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ABSTRACT

Bioactive substances are non-nutrient compounds primarily derived from plant-based foods that significantly modulate metabolic processes and confer health benefits beyond traditional nutritional functions. They include a wide range of compounds such as polyphenols, carotenoids, phytosterols, and glucosinolates, which have garnered substantial attention in nutritional science and medicine due to their potential roles in disease prevention and health promotion. This paper provides a comprehensive overview of the major classes of bioactive substances, their mechanisms of action, sources, and implications for human health. Furthermore, the discussion emphasizes the public health strategies that can utilize these compounds, emerging research trends, and future directions in bioactive substance research. Importantly, this review also extends to the application of bioactive substances in sustainable agriculture, highlighting their roles in plant–microbe interactions (notably with mycorrhizal fungi), soil health, natural pest suppression, and crop resilience under abiotic stress. These agricultural dimensions offer pathways toward reduced synthetic inputs and integration with renewable-energy-based farming systems.

Keywords
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I. INTRODUCTION

The intricate relationship between diet and health transcends the mere provision of essential nutrients, spotlighting a complex tapestry of biochemical interactions that significantly influence health outcomes. In recent decades, scientific inquiry has increasingly focused on bioactive substances---compounds within foods that exert biological effects at relatively low concentrations [1]. These non-essential compounds, often termed phytochemicals, exhibit diverse molecular structures and physiological functions that are crucial for reducing chronic disease risk and optimizing health [2].

Public health initiatives increasingly advocate a "food as medicine" paradigm, positioning plant-based diets rich in bioactive substances as critical strategies for chronic disease prevention. Multiple studies consistently find that higher consumption rates of such dietary patterns correlate with reduced incidences of complex chronic conditions, including cardiovascular disease, certain cancers, diabetes, and obesity [3]. A comprehensive understanding of the nature, distribution, and mechanisms of action of these substances is essential for developing evidence-based dietary guidelines, informing public health policies, and exploring therapeutic applications.

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This review first describes the main natural sources of bioactive substances (plants, microorganisms, algae, mycorrhizae), then addresses the major chemical classes and their mechanisms of action in human health, and finally discusses how these bioactive–organism interactions can be leveraged for sustainable agriculture. The overall aim is to provide a critical, rather than purely descriptive, synthesis – highlighting evidence quality, controversies, and knowledge gaps

II. ORIGINS OF BIOACTIVE SUBSTANCES

Bioactive substances are an integral component of our food system, originating from a variety of sources, including plants, microorganisms, algae, and fungi. These compounds play crucial roles in interactions with human health and the environment.

1. Plant-derived bioactive compounds

Plants are the primary sources of bioactive substances, synthesizing these compounds as part of their defense mechanisms. The two main classes of compounds derived from plants include:

Secondary metabolites: These are non-essential for the plant's basic survival but serve important ecological functions. They can deter herbivores, attract pollinators, and inhibit the growth of competing plants. Major groups of secondary metabolites include:

- Polyphenols: Found in high concentrations in fruits, vegetables, tea, and red wine, polyphenols such as flavonoids and phenolic acids have been extensively studied for their antioxidant and anti-inflammatory properties [4]. They are produced as a response to environmental stressors, such as UV exposure and pathogen attacks [1].
- Carotenoids: These pigments are responsible for the vibrant colors of many fruits and vegetables. Carotenoids offer protection against oxidative stress and UV damage and may be involved in various physiological processes [5].

Essential oils and alkaloids: Other classes of bioactive compounds include essential oils (terpenes and terpenoids) found in aromatic herbs, and alkaloids (e.g., caffeine, quinine) with potential therapeutic effects [3].

2. Microorganisms

Microorganisms, including bacteria and fungi, are another rich source of bioactive substances. They play a crucial role in nutrient cycling and can produce a variety of bioactive compounds that influence human health.

Bacteria: Many beneficial effects attributed to probiotics stem from the production of bioactive compounds such as short-chain fatty acids (SCFAs) during fermentation [6]. These compounds help regulate gut health, enhance the immune response, and even influence mood and cognitive functions. For instance, certain Lactobacillus and Bifidobacterium species produce compounds that exhibit antimicrobial properties [7].

Fungi: Various fungal species produce secondary metabolites known as mycotoxins, many of which have therapeutic properties. For instance, mycophenolic acid, produced by *Penicillium* species, is an immunosuppressant used in organ transplantation [8]. Moreover, mushrooms like Shiitake and Reishi contain polysaccharides (e.g., beta-glucans) that enhance immune function [9].

Algae: Algae represent a diverse group of photosynthetic organisms, encompassing both microalgae and macroalgae (seaweeds). These organisms are a treasure trove of bioactive compounds, including:

- Phycobiliproteins: Found in red algae and cyanobacteria, these proteins have antioxidant properties and are used as natural food colorants [10].
- Omega-3 Fatty Acids: Some microalgae are rich sources of omega-3 fatty acids (e.g., EPA and DHA), which are essential for human health and play significant roles in cardiovascular and cognitive functions [11].
- Polyphenols and Fucoxanthin: These compounds exhibit anti-inflammatory and antioxidant properties, making algae a promising source of bioactive substances for improving human health [12].

Mycorrhizae: Mycorrhizal fungi form symbiotic relationships with plant roots, enhancing nutrient uptake, especially phosphorus, and improving plant health and stress tolerance. These fungi can also produce bioactive compounds that promote plant growth and enhance the plant's resistance to pathogens.

- Secondary Metabolite Production: Mycorrhizal fungi can influence the synthesis of secondary metabolites in plants, leading to enhanced production of bioactive compounds such as flavonoids and phenolics [13]. This interaction benefits not only the plants but also enhances the nutritional quality of the food produced.
- Health Implications: Understanding the role of mycorrhizal fungi in stimulating the production of bioactive compounds can guide agricultural practices aimed at boosting the nutritional content of crops and enhancing crop resilience against stressors [8].

III. CLASSIFICATION AND MAJOR GROUPS OF BIOACTIVE SUBSTANCES

1. Polyphenols

Polyphenols are among the most abundant and diverse classes of bioactive compounds, comprising over 8,000 identified structures [4]. Their health benefits stem from their antioxidant properties, capacity to modulate inflammation, and influence on various cellular processes.

Flavonoids: This subgroup, which constitutes the largest category of polyphenols, encompasses various classes including flavonols (e.g., quercetin, kaempferol), flavones (e.g., apigenin, luteolin), flavanones (e.g., hesperidin, naringenin), anthocyanins, and isoflavones. Flavonoids are primarily found in fruits, vegetables, tea, wine, and cocoa. Epidemiological studies consistently associate higher intake of flavonoids with reduced cardiovascular disease risk, attributing these benefits to antioxidant activity, improved endothelial function, and modulation of inflammatory pathways [14]. Recent meta-analyses suggest that flavonoids may also play a role in cognitive health, reducing the risk of neurodegenerative diseases such as Alzheimer's and Parkinson's [15].

Phenolic acids: Major subclasses include hydroxybenzoic acids (e.g., gallic acid, protocatechuic acid) and hydroxycinnamic acids (e.g., caffeic acid, ferulic acid), found abundantly in coffee, whole grains, and various fruits and vegetables [16]. Recent findings indicate that these compounds exhibit potent anti-inflammatory properties and may influence metabolic processes, suggesting their role in chronic disease management [10]. Resveratrol, a prominent phenolic compound in red wine and grapes, has been highlighted for its potential cardiovascular benefits and anti-aging properties, although conclusive evidence from human studies is still being evaluated [17].

Recent advances: New research is increasingly focused on the interactions between polyphenols and gut microbiota. The fermentation of polyphenols within the gut produces bioactive metabolites that may enhance the health benefits of these compounds. This growing field emphasizes the interconnectedness of diet, gut health, and systemic health outcomes, indicating that the benefits of polyphenols might be significantly amplified through interactions with gut microbial communities [6].

2. Carotenoids

Carotenoids, lipid-soluble pigments responsible for the vibrant colors of many fruits and vegetables, are another key class of bioactive compounds. Over 600 carotenoids have been identified, though only about 40 are regularly consumed in the human diet [5]. Their health benefits extend beyond their role as precursors of vitamin A.

Key compounds: Notable carotenoids include β-carotene, lycopene, lutein, and zeaxanthin. β-carotene is particularly abundant in carrots, sweet potatoes, and leafy greens, functioning as a precursor to vitamin A---essential for vision, immune function, and skin health [11]. Lycopene, primarily found in tomatoes and tomato products, has demonstrated potential protective effects against prostate cancer. It should be noted that most evidence for carotenoids in prostate cancer prevention (e.g., lycopene) derives from observational studies; RCTs have yielded mixed results, and confounding by other dietary factors cannot be excluded [12].

Health benefits: Carotenoids have also shown promising effects on eye health, especially lutein and zeaxanthin, which are concentrated in the macula of the eye and protect against age-related macular degeneration by filtering blue light and scavenging free radicals [18]. Moreover, emerging research suggests that carotenoids may play a protective role against skin damage from UV radiation, thereby improving skin appearance and reducing the risk of skin cancers [19].

3. Glucosinolates and isothiocyanates

Glucosinolates are sulfur-containing compounds found predominantly in cruciferous vegetables such as broccoli, cabbage, Brussels sprouts, and kale [20]. The unique aspect of these compounds is their conversion into biologically active forms, such as isothiocyanates and indoles, when plant tissues are damaged.

Mechanisms of action: Sulforaphane, a prominent isothiocyanate derived from glucoraphanin in broccoli, is recognized for its potent cancer-preventive properties. It enhances the body's detoxifying capacity through the induction of phase II detoxification enzymes, which assist in eliminating carcinogens and free radicals [13]. Indole-3-carbinol has also garnered attention for its role in modulating estrogen metabolism, potentially lowering the risk of hormone-related cancers [8].

Public health implications: The consumption of cruciferous vegetables correlates with a reduced risk of various cancers, especially colorectal cancer, reinforcing their significance in public health nutrition [21]. Promoting higher consumption of these vegetables in dietary guidelines may offer a straightforward yet effective strategy for cancer prevention.

4. Phytosterols

Phytosterols, structurally similar to cholesterol, occur naturally in vegetable oils, nuts, seeds, and whole grains [22]. Their function in managing cholesterol levels and promoting cardiovascular health has been widely studied.

Health outcomes: Phytosterols work by competing with cholesterol for absorption in the intestines, effectively lowering LDL cholesterol levels. Research shows that daily intakes of approximately 2-3 grams of phytosterols can reduce LDL cholesterol levels by around 10% [23]. The cholesterol-lowering efficacy of phytosterols has led to their incorporation into functional foods such as fortified margarines and yogurts, making them a practical public health tool in cardiovascular disease prevention [24].

Clinical applications: The growing awareness of phytosterols' health benefits aligns with recommendations from major cardiovascular health organizations to incorporate these compounds into dietary strategies aimed at managing cholesterol levels, particularly for those at risk of heart disease.

IV. MECHANISMS OF ACTION

Understanding the mechanisms of action for bioactive substances is crucial for grasping their health benefits, as these involve complex interactions with biological pathways.

1. Antioxidant activity:

Many bioactive substances, particularly polyphenols and carotenoids, serve as powerful antioxidants, scavenging reactive oxygen species (ROS) and reactive nitrogen species (RNS) that can damage cellular macromolecules, such as DNA, proteins, and lipids [25]. While the antioxidant capacity of these compounds is well-established, emerging research questions the significance of their direct antioxidant activity in vivo, highlighting the possibility that their metabolites may play more prominent roles in influencing cellular signaling and gene expression. While direct antioxidant activity is well demonstrated in vitro, the in vivo relevance remains debated because polyphenols are extensively metabolized, and their metabolites often reach lower concentrations than the parent compounds [26].

2. Modulation of cell signaling and gene expression:

Bioactive substances can interact with specific receptors, enzymes, and transcription factors to influence cellular function. For example, isothiocyanates from cruciferous vegetables activate the Nrf2 (nuclear factor erythroid 2-related factor 2) pathway, leading to upregulation of genes responsible for antioxidant defense and detoxification [27]. Additionally, polyphenols modulate inflammatory signaling by inhibiting the activation of NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells), which is vital for managing chronic inflammatory conditions [28].

3. Anti-inflammatory effects:

Chronic low-grade inflammation contributes to the pathogenesis of numerous diseases, including cardiovascular disease, type 2 diabetes, and cancer [29]. Many bioactive compounds exhibit anti-inflammatory properties by inhibiting pro-inflammatory enzymes (e.g., cyclooxygenase and lipoxygenase), suppressing cytokine production, and modulating inflammatory signaling pathways [7]. This highlights the importance of dietary patterns rich in bioactive compounds as a preventive strategy against chronic inflammation.

4. Effects on gut microbiota:

Recent investigations highlight the role of bioactive substances, particularly polyphenols, in modulating gut microbiota composition and functionality, which subsequently influences host metabolism and immune function [30]. Many polyphenols resist absorption in the small intestine, reaching the colon where they serve as substrates for microbial metabolism. This fermentation not only produces bioactive metabolites but may also facilitate the growth of beneficial gut bacteria, leading to improved health outcomes [6].

V. SYNERGISTIC INTERACTIONS BETWEEN BIOACTIVE SUBSTANCES

The concept of synergy refers to the interaction between two or more agents that results in a combined effect greater than the sum of their individual effects. In the realm of nutrition, this interaction between bioactive substances can significantly enhance health benefits, particularly when consumed as part of a whole food rather than in isolation.

1. Enhanced bioavailability:

One of the critical ways in which bioactive substances can exhibit synergy is through enhanced bioavailability. When different bioactive compounds are consumed together, they may influence the absorption and metabolism of one another.

Example: The consumption of vitamin C-rich foods (such as citrus fruits) alongside iron-rich plant foods (like legumes) enhances iron absorption due to the reducing effect of vitamin C on ferric iron, thus converting it to a more absorbable ferrous form [31].

2. Complementary mechanisms of action:

Many bioactive compounds exert their effects through complementary pathways that can amplify their health-promoting properties.

Polyphenols and Vitamins: For instance, vitamin E and polyphenols both possess antioxidant properties but work through different mechanisms. Vitamin E acts as a lipid-soluble antioxidant, protecting cell membranes, while polyphenols can regenerate vitamin E and enhance its protective effects [32]. The combined action can provide a more robust defense against oxidative stress compared to either compound alone.

3. Microbiome modulation:

The human gut microbiome plays a vital role in metabolizing bioactive compounds, and the interaction among various bioactive substances can influence microbial composition and activity.

Polyphenols and Fiber: Dietary fiber and polyphenols are both known to have prebiotic effects that promote the growth of beneficial gut bacteria. When consumed together, polyphenols can enhance the fermentation of fiber by gut microbial communities, resulting in increased production of short-chain fatty acids (SCFAs) that promote gut health and immune function [6].

4. Cancer prevention:

Synergistic interactions among bioactive compounds have been extensively studied for their potential roles in cancer prevention.

Cruciferous Vegetables: Compounds such as glucosinolates (found in cruciferous vegetables) work synergistically with other dietary polyphenols and vitamins to promote detoxification enzymes in the liver. For example, sulforaphane, a metabolite of glucosinolates, can enhance the effects of flavonoids in modulating pathways involved in cell cycle regulation and apoptosis [33].

VI. APPLICATION OF BIOACTIVE SUBSTANCES IN AGRICULTURE

Bioactive substances, particularly polyphenols, present a variety of applications in agriculture that can enhance crop production, improve pest and disease resistance, and promote sustainable farming practices.

1. Natural pesticides and herbicides:

Many polyphenols exhibit phytotoxic properties that can be utilized in developing natural pesticides and herbicides.

Plant defenses: Polyphenols act as natural defense compounds that plants produce in response to herbivore attacks and pathogen infections. For example, flavonoids can deter insects by affecting their feeding behavior and growth rates, which can be harnessed in organic farming to reduce reliance on synthetic pesticides [34].

2. Enhancing crop resistance:

Bioactive substances can improve the innate resistance of crops to various biotic and abiotic stresses.

Stress response: The application of polyphenol-rich extracts can bolster crop resistance to environmental stressors such as drought, salinity, and extreme temperatures. For instance, antioxidants involved in mitigating oxidative stress can significantly improve resilience during stressful conditions [35].

3. Soil health and fertility:

The incorporation of plant-derived bioactive substances can improve soil health and fertility.

Promotion of soil microbial activity: Compost or biostimulants rich in polyphenols can enhance microbial diversity and activity in the soil, promoting nutrient cycling and organic matter decomposition. Beneficial microorganisms thrive in the presence of polyphenols, leading to improved soil structure and fertility [36].

4. Post-harvest treatments:

Polyphenols play a crucial role in enhancing the shelf life and quality of agricultural products post-harvest.

Antioxidant properties: The application of polyphenols can reduce oxidative damage in fruits and vegetables, thereby prolonging their shelf life. This is particularly useful in extending the freshness of produce during transportation and storage, as polyphenols can inhibit enzymatic browning and maintain color, texture, and nutritional quality [37].

Disease resistance: Polyphenols may also inhibit the growth of spoilage microorganisms and pathogens in harvested produce. This reduces the incidence of post-harvest diseases, contributing to lower food loss and waste [38]. By combining polyphenols with mycorrhizal fungi, farmers can create a more resilient crop that retains its quality throughout the supply chain.

5. Sustainable agricultural practices:

The integration of bioactive substances into agricultural practices aligns with the principles of sustainable agriculture.

Reduced chemical inputs: Utilizing natural bioactive compounds can decrease the reliance on synthetic fertilizers and pesticides, promoting environmental sustainability. This practice supports biodiversity and helps in maintaining ecosystem balance [39].

Organic farming: The application of polyphenol-rich practices supports the principles of organic farming, fostering soil health, enhancing biodiversity, and promoting natural pest management strategies.

6. Bioactive substances in the rhizosphere and nutrient cycling:

Beyond direct plant effects, bioactive substances (particularly root-exuded flavonoids and phenolic acids) shape rhizosphere microbial community composition and function. These compounds can :

Mobilize nutrients: for example, root exudates release phosphorus from insoluble mineral forms, reducing dependence on phosphate fertilizers [36].

Enhance biological nitrogen fixation: Flavonoids act as signaling molecules in legume–Rhizobium symbiosis, improving nitrogen inputs in low-fertilizer systems.

Suppress soil-borne pathogens: Glucosinolate breakdown products (isothiocyanates) from brassica green manures – a practice known as biofumigation – reduce soil pathogen loads and nematode populations, decreasing the need for chemical fumigants.

7. Linking bioactive substance use to renewable-energy-based and low-input farming systems:

The application of bioactive substances aligns with renewable-energy-based agriculture by reducing the energy-intensive production of synthetic agrochemicals. For example : - biopesticides and bioherbicides derived from plant phenolics require less fossil energy to manufacture than conventional synthetic counterparts; Mycorrhizal inoculation enhanced by polyphenol-rich biostimulants improves crop nutrient and water use efficiency, thereby lowering the energy demand for irrigation and fertilizer production and crop residues rich in bioactive compounds (e.g., glucosinolates from brassicas) can be integrated into circular bioeconomy models, where they serve both as soil amendments and as natural pest control agents.

VII. IMPLICATIONS OF POLYPHENOL-MYCORRHIZAL INTERACTIONS FOR ARID AGRICULTURE

The synergy between polyphenols and mycorrhizal fungi presents significant implications for arid agriculture, where water scarcity and nutrient limitations are major challenges.

Enhanced water use efficiency: The ability of mycorrhizal fungi to increase water absorption capabilities is invaluable in arid regions. Polyphenols can regulate plant responses to drought stress and minimize water loss, together improving water use efficiency [40].

Improved nutrient availability: Mycorrhizal fungi enhance phosphorus uptake, an important nutrient often limited in arid soils. The synergy with polyphenols may help solubilize important nutrients, ensuring plants are adequately nourished [41].

Soil health: Mycorrhizal fungi promote beneficial soil microbial communities, which enhance organic matter decomposition and nutrient cycling. Polyphenols may support these microbial populations, thereby contributing to healthier, more fertile soil in arid regions [42].

Resilience to stress: Through their interaction, polyphenols and mycorrhizal fungi can enhance plant resilience to environmental stresses, including salinity and heat. This can lead to improved yields and stability in arid agricultural systems While the beneficial effects of mycorrhizal fungi and polyphenols are well established under controlled greenhouse conditions, field validation in arid environments remains limited. Variability in soil texture, indigenous microbial competition, and climatic fluctuations can substantially influence outcomes. Future research should prioritize multi-site field trials and meta-analyses to distinguish robust effects from context-dependent responses. [43].

VIII. CONCLUSION

The integration of bioactive substances, particularly polyphenols, and their interactions with mycorrhizal fungi represent a promising frontier in the field of agriculture. From enhancing nutrient uptake and water efficiency to providing natural pest control and improving post-harvest quality, the applications are diverse and impactful. As agricultural practices increasingly shift toward sustainability, leveraging these natural compounds can lead to healthier soils, improved crop resilience, and ultimately, food security in the face of climate change and environmental stressors. Future research focusing on these interactions will further illuminate the potential benefits and complexities, paving the way for innovative agricultural strategies.

Priority directions for future research:

1. From human health to agroecology: Investigate whether bioactive compounds with proven human health benefits (e.g., specific polyphenols) can be enriched in food crops through targeted mycorrhizal or agronomic management; creating a direct link between agricultural practice and nutritional quality.

2. Level field validation: move beyond pot experiments to multi-year, multi-site field trials that assess the combined effects of mycorrhizae and polyphenol-rich amendments on yield stability, soil carbon, and reduction in synthetic inputs.
3. Bioactive–bioenergy integration: Explore the use of bioactive-rich crop residues (e.g., from glucosinolate-containing oilseeds) as dual-purpose materials for both soil conditioning and feedstock for renewable energy production (e.g., anaerobic digestion), aligning with circular bioeconomy principles.

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