Advanced Functional Materials and Bioactive Molecules

Applications in Environment, Health, And Industry

Editor
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Advanced Functional Materials and Bioactive Molecules: Applications in Environment, Health, and Industry

Modern scientific challenges increasingly transcend traditional disciplinary boundaries, demanding integrated approaches that connect chemistry, biology, materials science, environmental studies, and human health. This book is conceived as a comprehensive and interdisciplinary resource that explores how physicochemical properties, biological interactions, and functional materials converge to address issues of sustainability, ecosystem management, and biofunctional innovation.

Collectively, this book aims to provide researchers, graduate students, and professionals with a unified perspective on how physicochemical principles and biological processes interact across natural and engineered systems. By integrating marine science, bioinorganic chemistry, functional foods, advanced materials, and sustainable agriculture, the volume contributes to a holistic understanding of science-driven solutions for environmental resilience and human well-being.

Prof. Dr. Ferda ESER
Amasya University

İÇİNDEKİLER

CHAPTER 1

BIOLOGICAL INTERACTIONS AND BIOMATERIAL POTENTIALS OF POLYOXOMETALATES

SEDA CETINDERE[1]

1. Introduction

Polyoxometalates (POMs) represent a diverse class of discrete, anionic metal–oxide clusters composed primarily of early transition metals such as Mo, W, and V in their highest oxidation states. Their structural variability, well-defined redox behavior, and ability to incorporate heteroatoms or organic functionalities make them highly adaptable molecular platforms for advanced material design (Pope, 1983; Müller & et al., 1998). As outlined in numerous foundational studies, POMs exhibit tunable electrochemical properties and robust stability across a range of pH and solvent environments, positioning them as ideal candidates for functional biomaterials.

Over the past two decades, the intersection of POM chemistry and biomedical sciences has grown rapidly. Early observations of antiviral and antibacterial activity in

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heteropolyoxometalates provided initial evidence that these clusters could interact selectively with biological macromolecules (Yamase, 2005). Subsequent research revealed that POMs can modulate reactive oxygen species, inhibit key enzymatic pathways, or disrupt microbial membranes, thereby establishing a mechanistic basis for their biological actions (Rhule, Hill & Judd, 1998; Bijelic & Rompel, 2015). These biochemical capabilities—combined with their precise atomic-level architecture—have led to the exploration of POMs as enzyme mimics, therapeutic agents, drug delivery components, and hybrid bioactive materials.

Recent advances in materials chemistry have further enabled the integration of POMs into nanoscale carriers, polymeric matrices, and organic–inorganic hybrid frameworks. These engineered constructs enhance biocompatibility, improve pharmacokinetics, and allow stimuli-responsive behavior, significantly expanding the functional landscape of POM-based biomaterials (Chang & et al., 2022; Wang & et al., 2024).

Given their structural precision, adaptability, and rich electronic properties, POMs now stand as emerging building blocks for next-generation biomaterials. This chapter provides a comprehensive overview of biological interactions, and material design principles to establish a foundation for understanding their expanding roles across modern biomedical applications.

2. Biological Interactions of POMs

POMs exhibit a wide spectrum of biological interactions, which are central to their utility as bioactive materials. Their activity arises from a combination of electrostatic interactions, redox reactivity, and the ability to coordinate or disrupt biomolecular structures such as proteins, nucleic acids, and membranes (Rhule, Hill & Judd, 1998; Yamase, 2005). Understanding these interactions at the molecular and cellular level is crucial for the rational design of POM-based biomaterials for therapeutic, diagnostic, and regenerative applications.

POMs strongly interact with proteins via electrostatic and hydrogen-bonding interactions. The highly negative charge of POM clusters allows binding to positively charged residues (lysine, arginine) on protein surfaces, which can induce conformational changes or stabilize specific protein structures (Bijelic & Rompel, 2015). These interactions have been exploited in protein crystallography to improve crystal formation, but they also underpin potential biomedical applications, such as enzyme inhibition or stabilization, and modulation of signaling proteins (Miras, Wilson & Cronin, 2014). Metal-substituted POMs can mimic enzymatic active sites, acting as catalysts in redox reactions, hydrolysis, or phosphorylation processes, thereby functioning as artificial enzymes.

POMs interact with nucleic acids through electrostatic attraction to the phosphate backbone and through potential intercalation into DNA or RNA structures. These interactions can result in inhibition of nucleic acid replication or transcription, which contributes to the observed antiviral and anticancer activities (Yamase, 2005; Bijelic & Rompel, 2015). Certain lacunary and transition-metal-substituted POMs show selective binding to DNA structures, providing a basis for therapeutic targeting and controlled drug delivery.

The anionic nature and amphiphilic modification of POMs allow interaction with lipid bilayers. POMs can disrupt microbial membranes, leading to antibacterial and antifungal activity, or modulate the permeability of eukaryotic cell membranes to enhance cellular uptake of therapeutic cargos (Rhule, Hill & Judd, 1998). Surface-functionalized POMs incorporated into nanoparticles or polymeric carriers enhance membrane interaction while maintaining biocompatibility.

A key feature of POMs is their capacity to act as multielectron redox reservoirs. This property enables modulation of intracellular reactive oxygen species (ROS), contributing to anticancer, antioxidant, or pro-oxidant effects depending on context (Liu & et al., 2022; Carvalho & Aureliano, 2023). Redox-active POMs can catalyze selective oxidation of biomolecules or mediate electron transfer processes in artificial enzymatic pathways, demonstrating utility in both therapeutic and diagnostic platforms.

Cellular internalization of POMs occurs predominantly via endocytosis, with uptake efficiency influenced by cluster size, charge density, and surface functionalization (Geisberger & et al., 2013). Encapsulation or conjugation with organic ligands, peptides, or polymers improves stability in physiological media, reduces nonspecific interactions, and enhances targeted delivery. Understanding these pharmacokinetic factors is critical for designing POM-based biomaterials with controlled biodistribution and minimal cytotoxicity.

The diverse modes of POM–biomolecule interaction—spanning proteins, nucleic acids, membranes, and redox processes—provide a rich toolkit for biomedical application. Rational design leveraging structural functionalization, hybridization, and supramolecular assembly allows tailoring these interactions for specific therapeutic or diagnostic outcomes, setting the stage for POMs as multifunctional biomaterials.

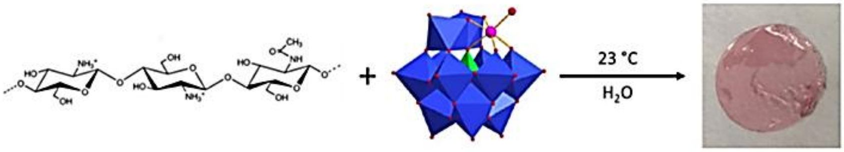
3. POMs in Biomaterials Engineering

The integration of POMs into biomaterials represents a critical step in translating their unique chemical and biological properties into functional platforms for biomedical applications. By combining the intrinsic redox activity, structural precision, and bioactivity of POMs with organic or inorganic scaffolds, researchers have developed multifunctional materials capable of drug delivery, antimicrobial activity, enzyme mimicry, and responsive behavior under physiological conditions (Bijelic & Rompel, 2015; Chang & et al., 2022; Wu & et al., 2023; Li & et al., 2023; Gubta, Sharma & Singa, 2024).

POM-Based Hydrogels

Hydrogels are three-dimensional, water-swollen polymeric networks widely used in tissue engineering, wound healing, and controlled drug delivery. Incorporation of POMs into hydrogels imparts redox functionality, antibacterial activity, and the potential for stimuli-responsive behavior (Liu & et al., 2022; Zhang & et al., 2020; Wang & et al., 2024; Al-Ghaus & et al., 2021). POMs can be physically entrapped within polymer networks or covalently linked to the polymer backbone. For example, Keggin-type POMs incorporated into poly(vinyl alcohol) or chitosan hydrogels have demonstrated enhanced antimicrobial efficacy and controlled release of encapsulated drugs (Figure 1.) (McWilliams & et al., 2024).

Figure 1. An example for POM-based hydrogels (McWilliams & et al., 2024).

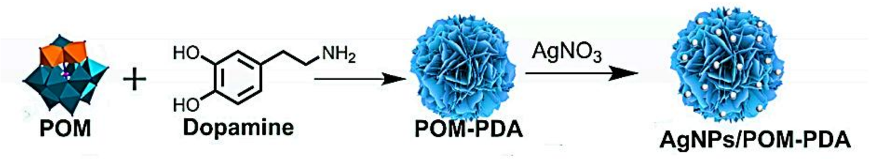


POM-Doped Polymeric Scaffolds

Synthetic and natural polymers, including poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), and gelatin, serve as scaffolds for tissue engineering. POM functionalization introduces redox activity and bioactive properties to these materials without compromising mechanical integrity (Chang & et al., 2022; Zhao & et al., 2022; Khan, Ahmed & Rehman, 2024; Liu & et al., 2023).

Metal-substituted or lacunary POMs have been used to create scaffolds that promote osteogenic differentiation and prevent bacterial colonization, highlighting the dual role of POMs in regenerative medicine and infection control (Taghiyar, Yadollahi & Abbasi Kajani, 2022). An example for POM-doped polymeric scaffolds is given in Figure 2. (Zhao & et al., 2022).

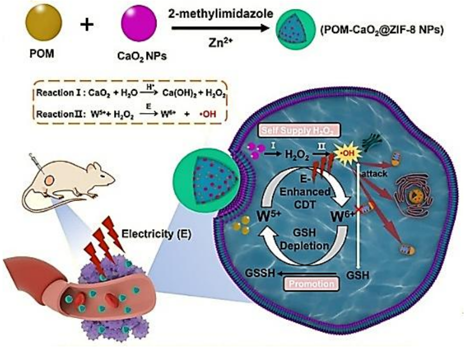
Figure 2. An example for POM-doped polymeric scaffolds (Zhao & et al., 2022).



POM-Functionalized Nanoparticles

Nanoparticles functionalized with POMs offer advantages in targeted drug delivery, photothermal therapy, and imaging. Electrostatic or covalent conjugation of POMs to polymeric, lipid, or inorganic nanoparticles enhances stability in biological media and allows for controlled cellular uptake (Sun & et al., 2022; He & et al., 2024). For instance, POM-decorated gold nanoparticles have been employed as multifunctional platforms combining photothermal cancer therapy with ROS-mediated cytotoxicity, demonstrating the potential for synergistic therapeutic strategies (Yamase, 2005). An example study for POM-functionalized nanoparticles was given in Figure 3. (Sun & et al., 2022).

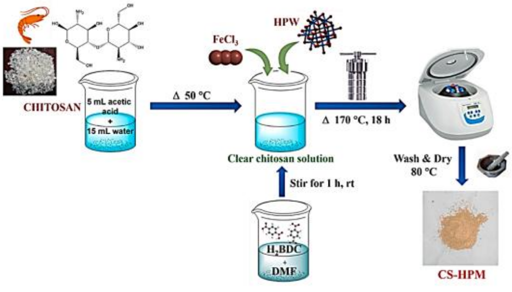
Figure 3. An example study for POM-functionalized nanoparticles (Sun & et al., 2022).



Hybrid POM–Biopolymer Conjugates

Hybrid materials combining POMs with biopolymers, such as peptides, polysaccharides, or proteins, exploit the complementary properties of each component. POMs confer redox and bioactive functionality, while biopolymers improve biocompatibility, degradability, and targeting potential (Miras, Wilson & Cronin, 2014; Bhuyan & Ahmaruzzaman, 2025). These conjugates have been applied in anticancer therapies, antimicrobial coatings, and enzyme-mimetic systems, offering customizable platforms for next-generation biomaterials. An example for hybrid POM–biopolymer conjugate was given in Figure 4. (Bhuyan & Ahmaruzzaman, 2025).

Figure 4. An example study for hybrid POM–biopolymer conjugate (Bhuyan & Ahmaruzzaman, 2025).



POM-based biomaterials span a broad spectrum of applications, from hydrogels and polymeric scaffolds to nanoparticles and bioceramics. Functionalization strategies—including covalent attachment, encapsulation, hybrid conjugation, and surface immobilization—allow precise control over biological interactions, stability, and therapeutic efficacy. These advances highlight the versatility of POMs as modular building blocks for engineering multifunctional biomaterials capable of addressing complex biomedical challenges.

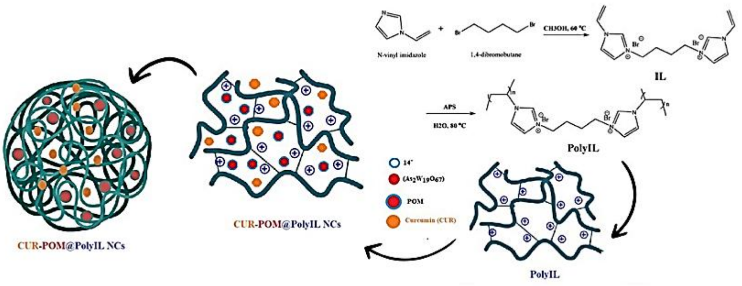
4. Biomedical Applications of POMs

POMs have demonstrated a wide range of biomedical applications due to their structural versatility, redox activity, and inherent biological interactions. These applications span anticancer therapy, antimicrobial treatments, antiviral interventions, enzyme inhibition, and diagnostic platforms. By combining functionalization strategies and engineered biomaterial scaffolds, POMs are increasingly recognized as multifunctional platforms in translational medicine (Yamase, 2005; Bijelic & Rompel, 2015; Cheng & et al., 2022).

Anticancer Applications

POMs exhibit selective cytotoxicity against cancer cells through multiple mechanisms, including reactive oxygen species (ROS) generation, mitochondrial disruption, DNA binding, and inhibition of cellular enzymes (Yamase, 2005). Metal-substituted and lacunary POMs have shown potent pro-apoptotic activity while minimizing effects on normal cells. Additionally, POM-based nanoparticles and hydrogel carriers enable targeted delivery, enhancing efficacy and reducing systemic toxicity (Azizullah & et al., 2018; Mohajer & et al., 2024). Hybrid POM-biopolymer conjugates further improve cellular uptake and tumor selectivity, providing promising avenues for combination therapy (Mousavi & et al., 2022; Khoshkhan & et al., 2024). An example study for anticancer applications was given in Figure 5. (Mohajer & et al., 2024).

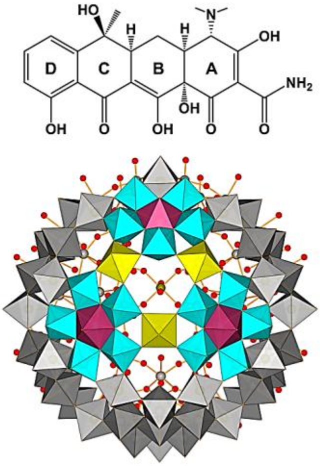
Figure 5. An example study for anticancer applications of POMs (Mohajer & et al., 2024).



Antimicrobial and Antiviral Applications

The anionic nature of POMs allows disruption of bacterial membranes, inhibition of microbial enzymes, and interference with viral replication (Dana & et al., 2019; Mousavi & et al., 2022; Zhao & et al., 2025). Keggin- and Dawson-type POMs have demonstrated activity against Gram-positive and Gram-negative bacteria, fungi, and enveloped viruses (Rhule, Hill & Judd, 1998; Yamase, 2005). Encapsulation of POMs in polymeric or lipidic carriers enhances stability under physiological conditions, facilitating long-term antimicrobial coatings for medical devices, wound dressings, and surface disinfectants. An example study for antimicrobial applications was given in Figure 6. (Grzhegorzhevskii & et al, 2023).

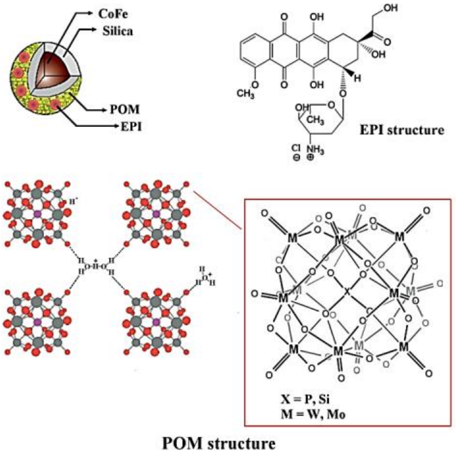
Figure 6. An example study for antimicrobial applications. (Grzhegorzhevskii & et al, 2023).



Drug Delivery Systems

Functionalized POMs integrated into hydrogels, nanoparticles, or polymeric scaffolds act as drug carriers with controlled release profiles. Their redox responsiveness and pH-sensitive behavior allow site-specific release of therapeutic agents, improving bioavailability and reducing off-target effects (Taghiyar, Yadollahi & Abbasi Kajani, 2022; Li & et al., 2014). Conjugation with targeting ligands, such as peptides or antibodies, enhances cellular uptake and therapeutic specificity. An example study for drug delivery systems was given in Figure 7. (Rafiee & Rahpeyma, 2016).

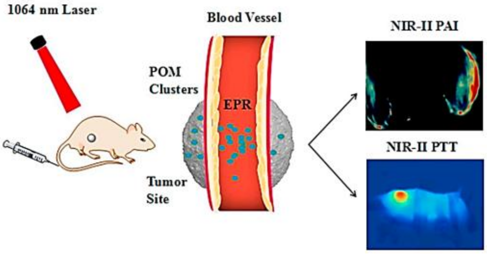
Figure 7. An example study for drug delivery systems. (Rafiee & Rahpeyma, 2016).



Diagnostic and Theranostic Applications

POMs can serve as imaging and biosensing agents due to their electronic transitions, redox activity, and ability to coordinate contrast-enhancing metals (Miras, Wilson & Cronin, 2014; Mousavi & et al., 2022; Khoshkhan & et al., 2024). Functionalized POM-nanoparticle hybrids have been employed for magnetic resonance imaging (MRI), fluorescence imaging, and photothermal therapy, enabling integrated diagnostic and therapeutic (“theranostic”) applications. These platforms exploit the intrinsic multifunctionality of POMs for real-time monitoring and controlled therapeutic intervention (Ni & et al., 2017; Han & et al., 2020; Kong & et al.; 2020). An example study for diagnostic and theranostic applications was given in Figure 8. (Han & et al., 2020).

Figure 8. An example study for diagnostic and theranostic applications. (Han & et al., 2020).



The biomedical applications of POMs illustrate their versatility as molecular building blocks and functional biomaterials. Through careful design and functionalization, POMs can be engineered to target cancer cells, inhibit pathogens, regulate enzymatic activity, deliver drugs, and provide diagnostic capabilities. The convergence of chemistry, materials science, and biology in POM research continues to expand their translational potential in modern medicine.

5. Challenges and Future Perspectives

POMs hold significant promise as multifunctional biomaterials due to their structural versatility, redox activity, and tunable biological interactions. However, several challenges must be addressed to fully realize their translational potential in biomedical applications. Despite the inherent stability of classical POM architectures such as Keggin and Dawson types, certain lacunary or vanadium-rich POMs can undergo hydrolysis, aggregation, or ligand exchange under physiological conditions (Pope, 1983; Yamase, 2005). Maintaining structural integrity in complex biological environments is critical for reproducible therapeutic efficacy. Strategies such as encapsulation within polymeric carriers, covalent conjugation with biopolymers, or supramolecular assembly have been explored to enhance stability and reduce cytotoxicity

(Khoshkhan & et al., 2024). Although functionalization strategies have improved the selectivity of POMs for cancer cells, bacteria, or specific enzymes, off-target effects remain a concern (Bijelic & Rompel, 2015). Future research must focus on advanced targeting mechanisms, including ligand-mediated recognition, stimuli-responsive release, and multi-modal targeting strategies, to maximize efficacy and minimize unintended interactions with healthy tissues.

Translating POM-based biomaterials from laboratory research to clinical applications requires scalable and reproducible synthetic routes. Challenges include controlling cluster size, composition, and functionalization at scale, as well as ensuring batch-to-batch consistency. Developing standardized, cost-effective, and environmentally sustainable synthetic methodologies will be essential for commercialization and clinical translation. While significant progress has been made in elucidating POM–biomolecule interactions, detailed mechanistic understanding at the molecular and cellular levels remains incomplete. Comprehensive studies on intracellular uptake pathways, redox modulation, enzymatic mimicry, and long-term bio-distribution are necessary to design rationally engineered POM-based biomaterials (Rhule, Hill & Judd, 1998; Miras, Wilson & Cronin, 2014).

Future perspectives in POM biomaterials research include:

- Multifunctional platforms: Combining therapeutic, diagnostic, and catalytic functions within a single POM-based material.
- Stimuli-responsive systems: Designing POMs that respond to pH, redox potential, or enzymatic triggers for controlled drug release.

- Hybrid and composite materials: Integrating POMs with nanomaterials, biopolymers, or 3D-printed scaffolds for regenerative medicine.
- Clinical translation: Advancing POMs toward preclinical and clinical studies, emphasizing safety, efficacy, and pharmacokinetics.

By addressing these challenges, POMs have the potential to become next-generation biomaterials capable of addressing complex biomedical problems with high precision and multifunctionality.

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CHAPTER 2

CAMELLIA SINENSIS TEAS AS FUNCTIONAL WINTER BEVERAGES FOR METABOLIC HOMEOSTASIS

ZEYNEB KARAKUŞ[1]

Introduction

During the winter months, teas such as ginger, rosehip, mountain tea, sage, echinacea, chamomile, cinnamon, mint, and lemon teas are commonly preferred because of their vitamin A and C content, trace minerals (iron, zinc, calcium), and strong antioxidant properties. However, teas produced from the leaves of *Camellia sinensis*-namely black, green, and white tea-should not be overlooked, as this plant naturally contains flavonols (catechins), flavonol glycosides, tannins (including gallic acid), enzymes, alkaloids, nitrogen-containing compounds, pectic substances, pigments, vitamins, minerals, and volatile aromatic compounds. These components make *C. sinensis* derived teas important

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functional beverages in winter nutrition (Anonymous, 2018; Graham, 1992; Higdon & Frei, 2003; Parmar et al., 2012).

Tea is the most widely consumed drink in the world after water. In Türkiye, its cultivation began in 1924, and three species-*Camellia sinensis*, *Camellia assamica*, and *Camellia cambodiensis*-have been identified in its botanical classification. For promoting alertness and supporting metabolic activity, white, green, and black teas are all considered beneficial. Their stimulating effects are mainly attributed to caffeine. A 250-mL cup of black tea contains approximately 60-90 mg of caffeine, green tea 35-70 mg, and white tea 30-55 mg. A physiologically safe daily caffeine intake is generally considered to be 300-350 mg/day (approximately 3-5 mg/kg, with a maximum of 5-8 mg/kg). Tea is both universal-consumed across nearly all cultures-and local, because every region has its own cultivation, processing, and preparation practices. Despite such differences, all tea types share similar stimulant effects and contribute to both mental and physical vitality (Graham, 1992; Parmar et al., 2012).

Black, green, and white teas-produced from the leaves of *Camellia sinensis*-are comparable to other herbal teas in their contribution to health and well-being. Like many medicinal plants, tea contains glycosides, organic acids, alkaloids, vitamins, tannins, minerals, and even naturally occurring antibiotic-like compounds. Among its more than 4,000 phytochemicals, the most important are flavonoid-type polyphenols. Epigallocatechin gallate (EGCG) is recognized as the most potent of these polyphenols. A cup of green tea typically provides around 300 mg of flavonoids, while black tea contains roughly 250 mg-indicating that their antioxidant capacities are not dramatically different. Given its familiar taste and widespread cultural acceptance, black tea can also be recommended as a functional herbal beverage. Another advantage of tea is its lower caffeine content compared with coffee; cup for cup, tea contains approximately one-third less caffeine. Tea leaves also contain vitamins C and E; however, vitamin C begins to degrade at temperatures above 30 °C and therefore does not remain active during brewing (Graham, 1992; Higdon & Frei, 2003).

Figure 1. *Botanical illustration of Camellia sinensis, depicting the leaves, flowers, seed capsules, and shoot morphology.*

Source: Köhler's Medicinal Plants, 1887 (public domain).

In recent years, matcha tea -another derivative of *Camellia sinensis*- has gained significant global popularity due to its concentrated biochemical composition and distinctive preparation method. Unlike traditional brewed teas, matcha is consumed in powdered form, allowing the entire leaf to be ingested. This results in a much higher intake of polyphenols, chlorophyll, L-theanine, and other bioactive compounds. Its growing use in both traditional and contemporary nutrition practices reflects not only cultural trends but also an expanding scientific interest in its antioxidant capacity, cognitive effects, and metabolic benefits. As such, matcha represents an increasingly important addition to the spectrum of *Camellia sinensis*-based functional beverages, particularly in the context of winter nutrition (Kochman, 2020; Higdon & Frei, 2003; Sokary et al., 2022).

Biochemical and Antioxidant Properties of *Camellia sinensis*

Green tea, produced from the unfermented leaves of *C. sinensis,* is particularly valued for its preservation of natural polyphenols, especially catechins. These include EGCG, EGC, ECG, and EC, which exhibit antioxidant, anti-inflammatory, and metal-chelating properties. In addition to catechins, tea contains caffeine, theophylline, L-theanine, chlorophylls, minerals, aromatic volatiles, and flavonols such as quercetin and kaempferol. Together, these compounds form the biochemical foundation of tea's health effects **(**Graham, 1992; Higdon & Frei, 2003; Parmar et al., 2012).

Tea polyphenols are powerful radical scavengers. They neutralize reactive oxygen species, inhibit lipid peroxidation, and enhance the activity of antioxidant enzymes. Studies in aging models show that green tea reduces oxidative stress markers and protects lipids and proteins from ethanol-induced damage. EGCG also provides neuroprotection by reducing beta-amyloid toxicity and modulating amyloid precursor processing. At the cardiovascular level, catechins inhibit oxidative modification of LDL cholesterol and improve endothelial function, contributing to decreased atherosclerotic risk. Green tea catechins have also shown antiproliferative and pro-apoptotic effects in various cancer cell lines, and long-term intake is associated with reduced cancer incidence in epidemiological studies. Additionally, green tea supports glucose control and improves insulin sensitivity in diabetic models. Overall, its catechin content makes tea one of the most potent antioxidant beverages available (Graham, 1992; Higdon & Frei, 2003).

Tea catechins also display antimicrobial activity. Hamilton-Miller (1995) reported that tea extracts inhibit Staphylococcus aureus, Salmonella, Shigella, Vibrio cholerae, and Streptococcus mutans. Catechins such as EGCG and ECG damage bacterial membranes and block virulence-related enzymes. Tea extracts also interfere with viral adsorption, demonstrating antiviral potential (Hamilton-Miller, 1995).

Matcha Tea: Biochemical Characteristics, Physiological Properties, and Its Role in Winter Nutrition

Matcha tea is a distinctive type of *Camellia sinensis* prepared by steaming and finely grinding shade-grown young leaves into a bright green powder. The most defining step of matcha production is the shading period applied 2-4 weeks prior to harvest. This practice increases the synthesis of chlorophyll and L-theanine, giving matcha its characteristic vibrant color and its unique umami-rich taste profile, which differs markedly from that of other teas. Another feature that sets matcha apart is that it is consumed as a suspension rather than an infusion; the powdered leaf is ingested directly without filtration. As a result, polyphenols, amino acids, vitamins, minerals, and plant pigments are delivered in substantially higher amounts compared with traditionally brewed teas (Kochman, 2020; Sokary et al., 2022).

The biochemical composition of matcha is particularly rich in catechins. Among these, EGCG, followed by EGC, ECG, and EC, plays a central role in reducing oxidative stress, modulating inflammatory pathways, and supporting metabolic functions. Shade cultivation markedly increases the L-theanine content of matcha leaves relative to other tea types. L-theanine modulates the effects of caffeine on the central nervous system, creating a unique neurophysiological balance that enhances mental clarity, focus, and calmness simultaneously. This synergy produces a smoother and more sustained stimulant effect compared with coffee (Kochman, 2020; Higdon & Frei, 2003).

Clinical and experimental studies indicate that matcha provides a broad range of physiological benefits. The strong antioxidant capacity of EGCG limits lipid and protein oxidation, protects cellular integrity, and suppresses inflammatory signaling mechanisms such as NF-κB. The metabolic effects of matcha polyphenols include improved glucose tolerance, reduced postprandial glycemic response, increased fat oxidation, and stimulation of AMPK activity. These properties make matcha a functional support for metabolic balance during winter, when physical activity may decline and detoxification slows. From a neurocognitive perspective, the combined effects of L-theanine and caffeine enhance attention, memory performance, and reaction time, making matcha a favorable beverage for mentally demanding tasks (Kochman, 2020; Sokary et al., 2022).

Matcha tea also contributes to detoxification due to its high chlorophyll and carotenoid content. The density of these pigments not only enhances antioxidant activity but also improves their bioavailability because the entire leaf material is consumed. In this regard, matcha represents not just a caffeine- or catechin-based beverage but a concentrated source of diverse phytochemicals (Kochman, 2020).

Nevertheless, certain considerations are necessary when consuming matcha. Because *Camellia sinensis* can absorb heavy metals from the soil, low-quality, unregulated products may contain contaminants such as lead or arsenic. For this reason, it is advisable to choose matcha from reliable, certified sources that undergo laboratory testing. Although its caffeine content is comparable to that of black tea, individuals sensitive to caffeine may experience insomnia or palpitations (Sokary et al., 2022).

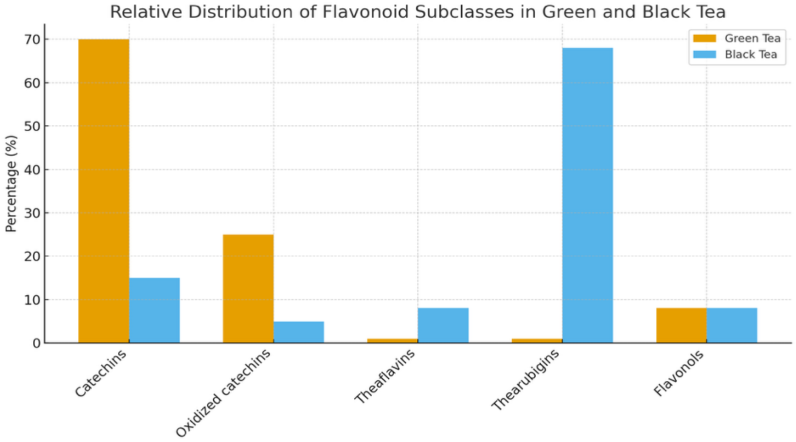
In conclusion, matcha-with its high polyphenol concentration, the neurophysiological balance created by L-theanine and caffeine, and its superior bioavailability-supports metabolic homeostasis, mental vitality, and antioxidant defense during winter. Both traditional use and modern scientific findings highlight matcha as a uniquely valuable tea variety within winter nutrition (Kochman, 2020; Sokary et al., 2022).

Differences Between Black, White, Green, and Matcha Tea

Although black, green, white, and matcha teas all originate from *Camellia sinensis*, they differ markedly in their processing techniques, biochemical composition, and sensory profile. Black tea undergoes full oxidation, during which catechins transform into theaflavins and thearubigins-compounds that deepen the color and intensify the flavor. Green tea, by contrast, is heated immediately after harvest to halt enzymatic oxidation, preserving the high catechin content characteristic of unfermented leaves. White tea, composed of unopened buds that are only withered and gently dried, represents the least processed form and therefore retains its native polyphenols to the greatest extent (Graham, 1992; Higdon & Frei, 2003; Parmar et al., 2012).

Matcha tea is produced through a distinctly different method. Prior to harvest, the plants are shaded for several weeks, increasing chlorophyll and L-theanine levels and resulting in the characteristic vibrant green color and umami-rich flavor. Unlike other teas, matcha is consumed as a powdered suspension, allowing the entire leaf to be ingested. This leads to significantly higher bioavailability of polyphenols, pigments, amino acids, and micronutrients. These production and composition differences give each tea a unique aroma, texture, and biochemical profile, distinguishing them clearly despite their shared botanical origin (Kochman, 2020; Higdon & Frei, 2003; Sokary et al., 2022).

Graphic 1. *Relative distribution of flavonoid subclasses in green and black tea*



Source: Redrawn from Higdon & Frei, 2003

Brewing Methods of *Camellia sinensis* Teas

The method of preparing tea plays a decisive role in determining its antioxidant yield, caffeine extractability, aromatic integrity, and overall sensory quality. Because black, green, white, and matcha teas differ in their processing and biochemical composition, they also require different brewing conditions to preserve their characteristic properties. Water temperature, steeping duration, leaf grade, and the type of brewing vessel all influence the final infusion (Graham, 1992; Higdon & Frei, 2003).

Black tea, being the most oxidized form of *Camellia sinensis*, requires higher temperatures to release the theaflavins and thearubigins responsible for its color and robust flavor. For optimal extraction, freshly boiled water (95-100 °C) should be poured over the leaves and allowed to steep for three to five minutes. Shorter steeping results in a weaker infusion, while prolonged steeping increases tannin release and may lead to excessive bitterness without providing meaningful additional antioxidant gain. Porcelain or glass teapots are preferred to prevent metallic interference with flavor (Graham, 1992; Parmar et al., 2012).

Green tea, by contrast, contains heat-sensitive catechins that degrade when exposed to excessively high temperatures. To preserve EGCG and maintain a balanced flavor profile, green tea should be brewed with water cooled to approximately 70-80 °C and steeped for two to three minutes. Higher temperatures can cause over-extraction of tannins, producing an astringent taste and diminishing the bioavailability of catechins. Loose-leaf varieties may be infused multiple times, with later infusions often yielding smoother flavor and more evenly distributed polyphenols (Higdon & Frei, 2003; Graham, 1992).

White tea, the least processed form of *Camellia sinensis,* requires gentle brewing to extract its delicate aromatic compounds and preserve its native polyphenols. Water heated to 75-85 °C is ideal, and a longer steeping duration-typically four to five minutes-allows the buds to open fully and release their mild floral notes. Because white tea is composed of tender leaf buds, its infusion remains light even when brewed longer, and it rarely develops the bitterness associated with more oxidized teas (Graham, 1992).

Matcha, unlike the other tea types, is not brewed as an infusion but prepared as a suspension. The finely powdered leaf is whisked directly into hot water, allowing the entire plant material to be consumed. Traditional preparation involves sifting 1-2 grams of matcha into a bowl and adding 60-80 milliliters of water heated to 70-80 °C. Using a bamboo whisk (chasen), the mixture is vigorously whisked in an “M” or zigzag pattern until a fine foam forms, producing a smooth and creamy beverage known as usucha (thin tea). For a thicker, more concentrated preparation (koicha), 3-4 grams of matcha are blended with a smaller volume of water using slow kneading motions to achieve a dense, syrup-like consistency. Because matcha involves ingesting the entire leaf, both its polyphenol content and caffeine exposure are higher than those of conventional brewed teas (Kochman, 2020; Sokary et al., 2022).

Across all tea types, the freshness of the leaves, the quality of water, and the timing of consumption influence both taste and functional benefits. Freshly brewed tea offers the highest antioxidant activity, while prolonged standing promotes oxidation and diminishes flavor. Adding sugar can reduce antioxidant potential, whereas a small amount of lemon may stabilize polyphenols and enhance flavor without compromising nutritional value. Proper brewing not only preserves the biochemical richness of *Camellia* *sinensis* but also maximizes its contribution to winter health and well-being (Graham, 1992; Higdon & Frei, 2003).

Health Effects and Practical Considerations

Tea consumption is associated with a wide array of health-promoting effects, many of which stem from the flavonoids and catechins that remain active after brewing. Numerous studies show that regular tea intake enhances concentration and physical performance, supports memory, slows age-related cognitive decline, aids weight control, strengthens bone health, and contributes to periodontal and immune system function. Catechins exert protective effects on cardiovascular tissues, help regulate inflammatory responses, and play a role in reducing the risk of thrombosis, cataracts, and atherosclerosis. According to the University of Maryland Medical Center, consuming two cups of tea daily may not only lower cancer risk but may also reduce recurrence (Graham, 1992; Higdon & Frei, 2003).

Although different tea types vary in their processing, the antioxidant potential of green and black teas remains comparable, with a typical 250-mL cup providing 250-300 mg of polyphenols. Among these, EGCG stands out as one of the most potent naturally occurring antioxidants-20 to 30 times stronger than vitamins C and E. These bioactive compounds collectively help maintain metabolic balance, counter oxidative stress, and support general well-being during the winter months (Graham, 1992; Higdon & Frei, 2003).

Practical considerations also influence the health benefits of tea. Excessively hot tea may irritate mucosal tissues, and sweetened teas-particularly those containing refined sugar or industrial fructose syrups-can diminish antioxidant activity. Unsweetened tea is preferred, and natural alternatives such as stevia may be used when sweetness is desired. Contrary to common belief, adding lemon does not impair the absorption of iron from animal foods and may even enhance tea’s antioxidant capacity. Freshly brewed tea provides the highest polyphenol content, while decaffeinated products, tea bags, and bottled teas generally contain lower levels (Graham, 1992; Higdon & Frei, 2003; Müftüoğlu, 2015; Müftüoğlu, 2017).

Conclusion

Given its cultural familiarity and widespread use, black tea-along with green and white tea-can be considered an important winter beverage that supports metabolic homeostasis. Other herbal teas may also be used, provided that they meet quality standards. While some teas (such as ginger, fennel, or senna) exert rapid effects, others-including ginkgo, ginseng, rosemary, or mistletoe-require longer periods of regular consumption due to tissue-level biochemical adaptations. In winter, when sweating and fluid turnover decrease and detoxification slows, the regular intake of properly prepared and high-quality teas supports hydration, antioxidant defense, metabolic balance, and overall vitality across all age groups (Graham, 1992; Higdon & Frei, 2003; Parmar et al., 2012).

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CHAPTER 3

MAGNETIC-METAL ORGANIC FRAMEWORKS (MAGNETIC-MOF): ENZYME IMMOBILIZATION

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ELIF OZYILMAZ[2]

Introduction

Metal Organic Frameworks (MOFs)

Metal organic frameworks (MOFs) are a class of compounds composed of metal ions or clusters coordinated to organic ligands to form one-, two-, or three-dimensional structures. Metal–organic frameworks (MOFs) are organic–inorganic hybrid crystalline porous materials composed of a regular array of positively charged metal ions surrounded by organic 'linker' molecules (Ahmadi & et al., 2021). Metal ions form nodes that connect the arms of the linkers to form a repeating, cage-like structure. Because of this hollow structure, MOFs have an

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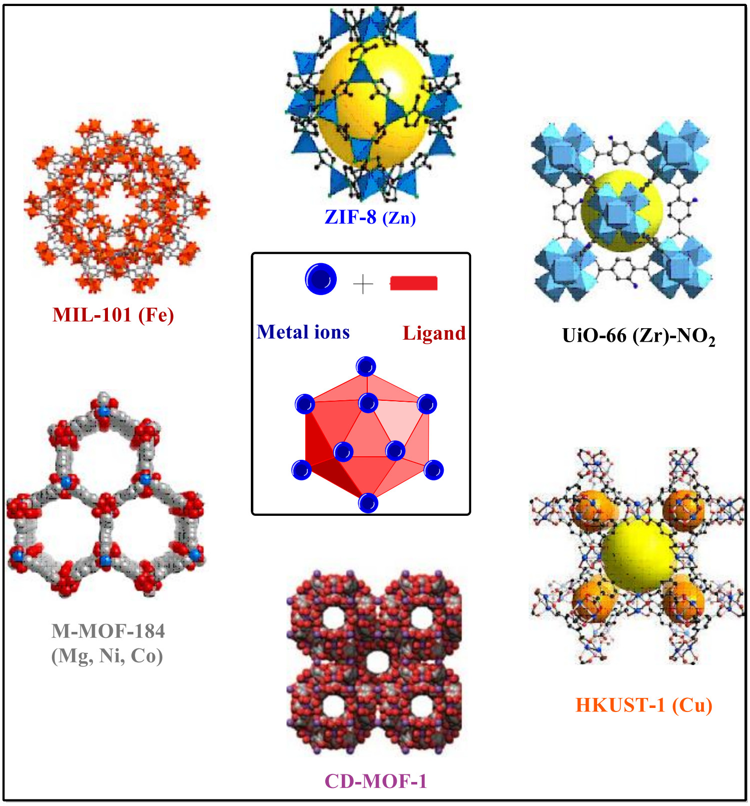
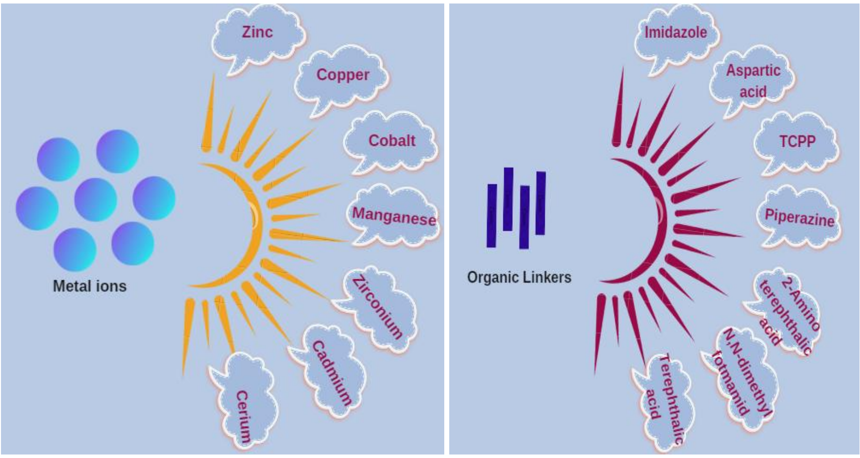
exceptionally large internal surface area. Metal-organic frameworks (MOFs), also commonly known as porous coordination systems, are a type of advanced materials that combine various inorganic ions with organic ligands to form a single, easily bonded structure that has attracted great attention due to its excellent physicochemical properties (Yildirim & et al., 2024). MOFs can be designed, tailored and modified with structural parameters such as metal clusters, organic linkers and pore sizes to achieve significantly high surface area, high porous crystal, high density of active sites and high stability, and due to these features, it is possible to successfully control MOFs (Kitagawa, 2014). While the unique structure design and tunability of MOFs is exciting, crystalline porous materials composed of both organic and inorganic components in a solid periodic network structure are not easily accessible in traditional porous materials such as fully inorganic zeolites. The physicochemical properties of materials are governed by the synergistic effects of structures and compositions, and MOFs are fascinating examples of how the unique structure of hollow-structured materials can provide a range of advantageous properties. These include improved surface-to-volume ratio; lower density; microreactor environment; higher loading capacities; and reduced mass and charge transport lengths (Hu, Masoomi & Morsali, 2019). As a result, the preparation of hollow structures for technological applications has long been a popular area of research for chemists and materials scientists. However, the controlled synthesis of porous or hollow materials with controllable and especially complex structures and a specific composition has always been a challenge for scientists. Pioneered in the late 1990s at UC Berkeley by Prof. Omar Yaghi ("Design and Synthesis of an Extraordinarily Stable and Highly Porous Metal-Organic Framework"), MOFs have become a rapidly growing area of research. To date, over 90,000 different MOF structures have been reported, and the number is growing (Zhou & et al., 2012). Numerous applications that exploit the cage-like structure of MOFs are being developed in many areas, including gas storage and separation, liquid separation and purification, electrochemical energy storage, catalysis, and enzyme immobilization. In addition to direct applications, MOFs have been used as unique precursors for the construction of inorganic functional materials with unique design possibilities, such as carbons, metal-based compounds, and their composites. Currently, carbonaceous materials have attracted great attention for their extensive applications including adsorption, catalysis, batteries, fuel cells, supercapacitors, drug delivery, and imaging, as well as techniques such as enzyme immobilization. Scientists have provided fundamentally new materials design tools by providing an approach such as enzyme immobilization for the design of numerous metal-organic framework (MOF) structures (Ozyilmaz, Ascioglu & Yilmaz, 2021a). These exciting materials have inspired a large number of scientists and engineers from various disciplines to explore their extraordinary work. Among these advanced materials, MOFs have been found to be superior to enzyme immobilization due to their high porosity, large surface area, and convenient synthesis. Furthermore, the high porosity and large surface area can be designed to control the degradation and release of biomacromolecules and living systems. Current research has revealed that the high chemical/physical stability of MOFs can help biomacromolecules and living systems withstand stress from organic solvents or extreme temperatures (Wang & et al., 2022; Ma & et al., 2024).

Figure 1. *Metal organic frameworks types.*



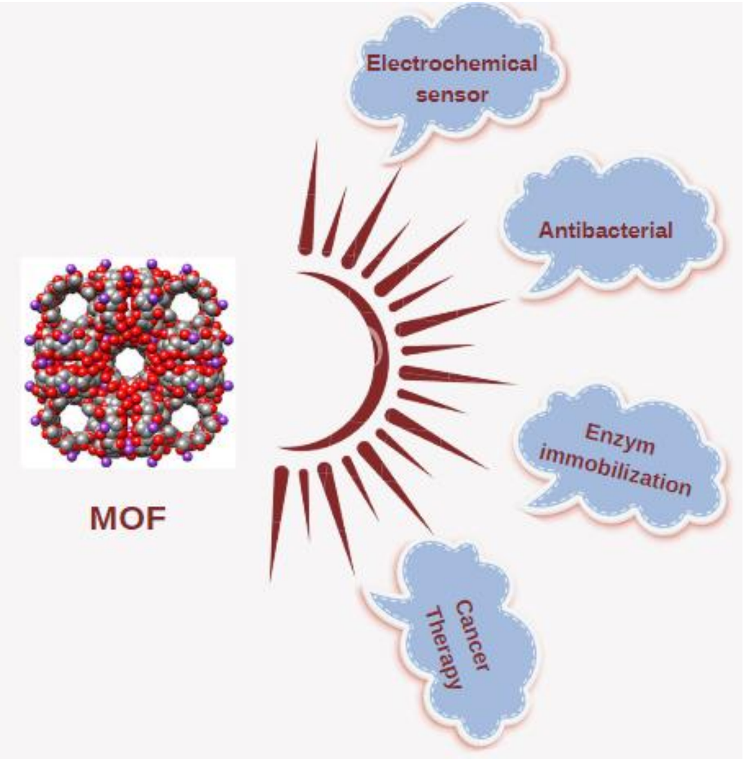
Zeolites are microporous crystalline solids with well-defined structures. They usually contain silicon, aluminum, and oxygen in their structures, and cations, water, or other molecules in their pores. Zeolites have many different crystalline structures, with large open pores (sometimes called cavities) in a very irregular arrangement, roughly the same size as small molecules. The most interesting thing about zeolites is their open, cage-like 'framework' structure and the way they can trap other molecules inside. MOFs are self-assembled metal clusters with organic ligands, their structure is well known for its permanent pores and tunable properties and have shown great promise for various applications. MOFs are structures composed of inorganic nodes, which can be single ions or ion clusters and organic linkers. They contain potential cavities that can be used for various applications. Organic linkers used in MOFs can connect two metal oxide clusters (ditopic linkers). Linkers with higher dimensionality can also be used. The bonds formed between the metal ions and the rotary atoms of the linker are strong and as a result the extended network structure in the MOF is quite rigid. The coordination complex formed by the metal ions and the rotary atoms of the linker, called secondary structure units, determines the final topology of the MOF framework. Transition metal ions are often used as inorganic components of MOFs (Manousi & et al., 2019).It is well known that different metal ions prefer different coordination numbers and geometries, such as linear, T- or Y-shaped, tetrahedral, square planar, square pyramidal, trigonal bipyramidal, octahedral, trigonal prismatic and pentagonal bipyramidal. Organic ligands with rigid backbones are often preferred because rigidity makes it easier to predict network geometry and, in addition, rigidity also helps maintain the open pore structure after removal of the incorporated solvent. Using the appropriate system, it is possible to synthesize extended polymeric or discrete-closed oligomeric structures. MOFs containing large cavities can result in the formation of interlocking structures. The formation of interlocking networks can be prevented by choosing appropriate organic ligands (Yan & et al., 2016).

Figure 2. *Various metal ions and organic binders used in the MOF structure.*



Careful selection of MOF components can give crystals ultra-high porosity and high thermal and chemical stability. The properties allow the interior of MOFs to be chemically modified for use in gas separation, gas storage, and catalysis, among other applications. Active sites on MOFs are located at metal nodes on the crystal structure; when reactions occur, the framework protects the active sites and increases efficiency (Amooghin & et al., 2022)

Figure 3. *Application areas of MOFs.*



Many Potential Applications of MOFs

Many potential applications of MOFs depend on the size and nature of the free volume or pores available in the framework structure. Tuning of the pores is typically achieved by changing metal ions or organic ligands. Extension of organic chains can result in increased pore size, but is usually limited by a decrease in the stability of the framework. In addition, the backbone of the compound is made up of metal ions that act as binders and organic bridging ligands that act as binders. In addition, the easily accessible porosity of MOFs and the presence of inorganic (hydrophilic) and organic (hydrophobic) parts together in the structure can affect the adsorption properties. Although most MOFs are electrical insulators, some materials have recently demonstrated excellent electrical conductivity and high charge mobility (Verma & et al., 2023). For better application areas of MOFs;

- Surface area: MOFs with higher surface area are more preferred.

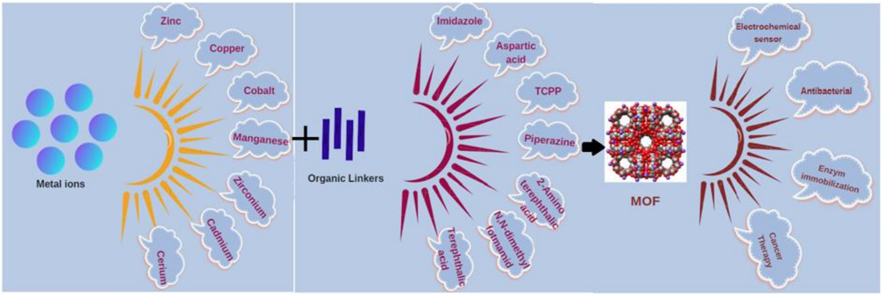
- Pore size: MOFs should have appropriate pore size to allow uptake and release of analytes.

- Stability: MOFs should exhibit reasonable stability when exposed to oxygen, moisture, analytes of interest or changes in temperature.

- Solubility: MOFs should not dissolve in aqueous media.

- Analyte interaction: MOFs may exhibit special structural features that can facilitate selective uptake and release of analytes. There are various synthesis methods of MOFs. These are generally hydrothermal/solvothermal, ultrasonic, electrochemical and encapsulation(Cota & Martinez, 2017; Kalmutzki, Hanikel & Yaghi, 2018).

Figure 4.*General demonstration of the use of MOFs in application areas.*



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Enzyme Immobilization

Enzymes are biologically derived biocatalysts with very high potential in various industrial areas due to their high selectivity, activity under mild conditions, and specificity (Garcia-Galan & et al., 2011). Twenty-first-century chemistry is expected to demand increasingly selective and cleaner processes, and in this context, enzymes are attracting considerable attention from researchers. They exhibit several interesting properties, such as high activity, high selectivity, and the ability to operate in more environmentally friendly solvents (usually water) at moderate physiological pH and temperature. Enzymes offer many advantages in the chemical industry, with potential applications ranging from small-scale fine chemicals and pharmaceuticals to large-scale energy and food industries (Dulebohn & et al., 2008; Patel & et al., 2008).

However, their biological origin makes enzymes less suitable for industrial use, and their applications often face challenges such as insufficient chemical and storage stability, difficult recovery, and limited reusability. Enzymes are generally soluble, inhibited by substrates, products, and other components, moderately stable, and lack ideal catalytic properties toward non-physiological substrates (Leresche & Meyer, 2006). Enzyme immobilization has been recognized as an important tool to overcome these disadvantages. Many strategies, including directed evolution, protein engineering, semi-rational/rational design, immobilization, and modification of reaction conditions, have been employed to increase enzyme efficiency. Among these strategies, enzyme immobilization is considered one of the most promising approaches (Qiao & et al., 2023).

Furthermore, immobilization enhances enzyme stability during storage and under operating conditions such as elevated temperature, organic solvents, or autolysis. It also facilitates the separation and reuse of enzymes while minimizing or eliminating protein contamination in the reaction medium, significantly reducing costs and enabling industrial applicability in continuous fixed-bed processes. Moreover, the reusability of immobilized enzymes results in higher catalyst efficiency (Ascioglu & et al., 2024a).

Magnetic–MOF for Enzyme Immobilization

Over the past two decades, enzyme immobilization has evolved into an effective method for enhancing enzyme activity and stability under extreme pH conditions and high temperatures. Various materials, including silica composites, sol–gels, and magnetic nanoparticles, have been used to immobilize free enzymes, making them not only easier to recycle and reuse but also easier to separate from the product. However, several limiting factors remain for immobilized enzymes, such as low loading efficiency, high leaching rates, and mass transfer resistance. Therefore, further efforts are needed to improve immobilization methods or to synthesize new, more efficient carriers (Gao & et al., 2021).

Enzyme immobilization can be achieved through simultaneous formation and immobilization in a magnetic-MOF assembly or by immobilizing the enzyme onto a pre-synthesized magnetic-MOF via physical interactions or chemical bonding. We classified the immobilization strategies into four categories: (i) physical adsorption onto magnetic-MOF, (ii) covalent bonding with magnetic-MOF, (iii) biomineralization, and (iv) one-pot encapsulation. The list of CRL enzymes immobilized on magnetic-MOF is summarized in Table 1 (Ascioglu & et al., 2024b).

Table-1*Enzyme immobilization by using varios magnetic (Fe_3O_4)-MOF@Enzyme materials.*

MOF	Metal	Ligand	Lipase source	Methotd	Ref
Fe_3O_4@Calix-ZIF-8	Zn^{2+}	2-Methylimidazole	CRL	One-pot encapsulation	(Ozyilmaz et al., 2021b)
mZIF-8@GOx	Zn^{2+}	2-Methylimidazole	GOx	Biomineralization method	(Hou et al., 2015)
Fe_3O_4@MOF	Fe^{3+}	Benzene-1,3,5-tricarboxylic acid	CRL	Covalent Bonding	(Wang et al., 2016)
Fe_3O_4@PDA@[$Cu_3(btc)_2$]	Cu^{2+}	Benzene-1,3,5-tricarboxylic acid	Trypsin	Physical adsorption	(Zhao et al., 2015)

In all enzyme immobilization examples, various metal ions have been used as inorganic components, while 2-methylimidazole and benzene-1,3,5-tricarboxylic acid are commonly employed as organic linkers during MOF formation around magnetic nanoparticles (typically Fe_3O_4). The choice of immobilization methodology should be based on preserving enzyme activity, efficiency, and stability. For encapsulation methods used in catalytic applications, it is important to consider the influence of the selected framework components, as they may affect substrate diffusion or selectivity.

Biomineralization Method

Biomineralization is a mineral deposition process mediated by organisms and represents one of the most important biomanufacturing technologies, widely explored in both intracellular and extracellular processes (Estroff, 2008). It is closely associated with the interactions between mineral precursors and biointerfaces and facilitates the *in situ* growth of inorganic minerals on a variety of biological templates, ranging from large organisms such as mussels to small-scale entities such as cells and proteins. From a structural perspective, a biomimetic mineral with high porosity is essential for exploiting the functions of internal biomacromolecules, as it can enhance mass transfer and provide high accessibility to these molecules. In this context, porous materials such as metal–organic frameworks (MOFs) are ideally suited for this purpose. Indeed, over the last decade, an increasing number of MOF-based approaches for biomimetic mineralization have been developed (Meldrum & Cölfen, 2008).Among these, zeolitic imidazolate frameworks (ZIFs), such as ZIF-8, have been prioritized due to their structural advantages, including high porosity, water stability, and mild crystallization conditions (e.g., aqueous media and room temperature), which are compatible with biomacromolecules. The mechanism of ZIF biomimetic mineralization is thought to be strongly related to the interfacial chemistry of the biomacromolecular template. To date, various proteins (including enzymes) and other biomolecules, such as hyaluronic acid, heparin, chondroitin sulfate, and dermatan sulfate, have been used as templates to initiate ZIF formation. In these examples, electrostatic interactions between negatively charged moieties on biomolecule surfaces and metal ion precursors (Zn^{2+}) mediate ZIF nucleation and govern the biomineralization process. Owing to these interfacial interactions, *in situ* synthesis of porous ZIF minerals has been extended to entire biological entities such as bacteria, cells, and tobacco mosaic viruses. These systems exhibit multifunctional properties at the intersection of chemistry and biology (Harding **&** et al., 2008; Zhang **&** et al., 2013b; Akkineni **&** et al., 2022).

The biomineralization approach imparts unexpected new functionalities to substrates. Biomimetic mineralization adapts self-assembly processes found in natural biological systems and applies them to the encapsulation of bioactive molecules, providing a protective external environment. This method has attracted considerable attention due to its rapid, simple, and mild immobilization procedure, which can lead to superior catalytic activity and remarkable operational stability. Therefore, biomimetic mineralization has been developed as an approach for hosting enzymes within metal–organic frameworks. Enzyme biomineralization involves mixing enzymes with MOF precursors.

The enzyme molecules act as structural units that facilitate nucleation of the porous crystal and induce rapid crystallization around the enzyme. They also promote the retention of enzymes within the MOF through hydrogen bonding and hydrophobic interactions (Xue **&** et al., 2024).

One-pot Encapsulation Method

Metal–organic frameworks (MOFs) are a class of crystalline hybrid porous materials synthesized from organic linkers and inorganic metal nodes through coordination bonds. Owing to their tunable pore size, customizable structure and topology, and water stability, the encapsulation of enzymes within MOFs has become an increasingly popular approach for enzyme immobilization and protection. Among them, zeolitic imidazolate framework-8 (ZIF-8) is one of the most attractive MOFs for enzyme immobilization due to its excellent biocompatibility (Farha **&** Hupp, 2010; Furukawa **&** et al., 2013).

Recently, to further simplify recovery processes in enzyme-catalyzed reactions, magnetic nanoparticles (MNPs) such as Fe_3O_4 have been encapsulated within enzyme-incorporated MOFs. The resulting magnetic framework composites (MFCs) can be easily recovered with minimal loss using an external magnetic field, while the recovered enzymes retain improved activity. Although promising, only a limited number of examples have been reported due to the complex procedures involved in MFC synthesis.

Furthermore, enzymes are often immobilized on the surface of MFCs with low loading efficiency, which may even result in enzyme aggregation or unfolding (Zhang **&** et al., 2013a; Zou **&** et al., 2020; Ji **&** et al., 2021).

Physical Adsorption

It is a simple, cost-effective, rapid, and widely used method for enzyme immobilization. Over the past decade, tremendous efforts have been devoted to preparing porous nanomaterials as supports for enzymes. The large surface area, pore diameter, and uniform pore size of MOFs have been widely investigated as potential features that make them suitable supports for enzyme immobilization. Furthermore, MOFs can exhibit strong interactions with enzymes—such as hydrophilic/hydrophobic and electrostatic interactions—thereby preventing enzyme leakage during operation.

Biocatalysis using natural enzymes is highly attractive for sustainable chemistry, as it minimizes waste and energy input due to the enzymes' high selectivity and reactivity under mild reaction conditions. Metal–organic frameworks (MOFs) are crystalline microporous networks formed by coordinating metal ions with organic linkers and are characterized by high surface area and easily tunable structures, pore sizes, and compositions. These properties make MOFs widely applicable in traditional porous-material technologies (e.g., molecular storage, separation, transport, and catalysis), while also qualifying them as excellent potential supports for enzymatic biocatalysis (Fried, Brieler & Froeba, 2013; Huo **&** et al., 2015).

Covalent Bonding

Among immobilization methods, covalently binding an enzyme to a carrier—i.e., forming covalent bonds between the enzyme and the support—has the advantage of firmly anchoring the enzyme and preventing its leaching from the support surface during reactions. Metal-ion affinity interactions, which exploit the zeta potential of the support and the opposite charges of enzymes, offer a straightforward immobilization approach and can be optimized to achieve ideal immobilization conditions. In addition to these inherent benefits, immobilization can also enhance lipase catalytic activity, likely due to conformational changes in the lipase molecules, opening of the active-site lid, and interfacial activation induced by the presence of hydrophobic substrates.Among various promising supports, magnetic nanoparticles (MNPs), most commonly Fe_3O_4, offer excellent opportunities for facile separation and repeated use. Fe_3O_4 nanoparticles are promising candidates due to their superparamagnetic behavior and high saturation magnetization. However, bare Fe_3O_4 nanoparticles are highly susceptible to oxidation and present a limited number of active sites for enzyme attachment. Metal–organic frameworks (MOFs), on the other hand, are highly ordered crystalline materials in which metal centers are bridged by multidentate organic ligands, forming low-density porous network structures with diverse topologies. MOFs have attracted substantial attention due to their tunable pore structures, functionalities, and high specific surface areas. These properties make them excellent supports for enzyme immobilization, as functional sites can coordinate with enzymes and the pores can encapsulate them to achieve high immobilization efficiency (Wang, Zhao & Yu, 2016).

Wang et al. reported that constructing a core–shell Fe_3O_4@MOF microsphere integrates the advantageous properties of both components into a single system, providing multiple functionalities beneficial for lipase conjugation. Although various core–shell materials based on zeolites, mesoporous oxides, polymers, and carbon materials have been explored as biocatalysts, magnetic MOFs have rarely been used as enzyme immobilization supports. Existing techniques often require surface modification with mercaptoacetic acid (MAA), which is highly toxic and can generate harmful gases when exposed to certain oxidants. Therefore, the current methods are unsuitable for use in enzyme immobilization (Banerjee & et al., 2012; Ke & et al., 2012; Ghasemi & et al., 2014).

Conclusion

As supports used to stabilize enzymes under harsh environmental conditions, MOFs have become attractive materials due to their excellent chemical and thermal stability. Moreover, MOFs are frequently employed in enzyme immobilization studies because of their lattice characteristics and highly porous structures. Although magnetic MOFs offer numerous advantages, various magnetic MOF composites also exhibit a wide range of applications in biocatalysis. The use of magnetic MOFs in enzyme immobilization enhances biocompatibility under mild reaction conditions. In addition, the selection of MOF synthesis methods is determined by the organic and inorganic solvents used, which depend on the requirements of biocatalytic applications. Further development is needed to create new opportunities for the rational design of multifunctional magnetic hybrid materials as platforms for enzyme immobilization. Such advancements could significantly enhance their potential applications in biochemistry and biotechnology.

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CHAPTER 4

PHYSICOCHEMICAL PROPERTIES AND POLLUTION DYNAMICS: IMPLICATIONS FOR BLACK SEA SMALL SCALE FISHERY MANAGEMENT

SINEM GOKTURK[1]
DIDEM GOKTURK[2]

Introduction

The Black Sea has existed for several million years and has been, and still is, one of the most interesting seas for biological and marine life research. Bulgaria, Georgia, Romania, Russia, Turkey, and Ukraine surround it. It serves as an important waterway for surrounding countries, carrying a variety of goods and raw materials. Tourism and fishing activities have been operating for many years on the Black Sea. The Black Sea does not benefit from the passage of millions of liters of water like the Atlantic and Pacific Oceans, and the surface water mixing rate is very low. The Bosporus Strait, connecting the Black Sea with the Marmara Sea and representing the border between the two continents of Europe and Asia, also provides a very low water exchange. Hence, the Black Sea, a unique marine ecosystem, faces significant threats from chemical pollution that adversely affect its fisheries. Therefore, the Black Sea has been

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subjected to increasing levels of chemical pollution due to industrialization, agricultural runoff, and urbanization. This pollution poses significant threats not only to the marine ecosystem but also to the livelihoods of communities dependent on fisheries. This paper examines the physicochemical properties of the Black Sea and investigates the impact of various forms of chemical pollutants, including heavy metals, pesticides, and industrial discharges, on fish populations and the broader marine environment. Through a synthesis of existing literature and data, this work highlights the urgent need for effective management strategies to mitigate pollution and protect the vital fishery resources of the region.

Basic Geographic and Physicochemical Characteristics of the Black Sea

The Black Sea, which lies between latitudes 40° 55′ and 46° 32′ north and longitudes 27° 27′ and 41° 42′ east, where the continents of Europe and Asia converge, is a semi-enclosed body of water bordered by six countries: Bulgaria, Romania, Ukraine, Russia, Georgia, and Turkey. It is characterized by its unique hydrological and ecological conditions, which support a diverse array of marine life, including commercially important fish species. Due to its location, it has the characteristics of an inland sea connected to the Mediterranean. It is a wide basin located between two large and different units, such as Anatolia and the Caucasus, which are generally formed by the Alpine orogeny, and the Eastern European platform, which is formed by lands before the First Geological Period (Sezgin et al., 2017; Oguz, Diaconescu, & Puzdrowska, 2020: 1475). The Black Sea, which is connected to the Sea of Marmara from the south by the Bosphorus Strait and to the Sea of Azov from the north by the Kerch Strait, has a maximum depth of around 2200 m (2206 ft) off the coast of Inebolu, Turkey (approximately 30-40 miles). The average depth is -1300 m, its surface area is 459064 km^2, including the Sea of Azov (36875 km^2), and its water volume is

537000 km^3. The distance between the extreme points in the east-west direction is 1149 km, and the maximum width in the north-south direction is 611 km. The narrowest section of the Black Sea is about 250 km between the Inceburun and Yalta shores of Sinop. The widest part is between the Black Sea entrance of the Bosphorus and the mouth of the Dnieper River (Figure 1).

Figure 1. Location map of the Black Sea (Anonymus, 2025).

The Black Sea basin can be divided into four separate physiographic units: continental shelf, continental slope, continental slope toe, and abyssal plain (deep water plain). However, the majority of it consists of the continental shelf and the continental slope in front of it. Although these units cover large areas in the northern part of the sea, they are very narrow on the Anatolian coasts. In contrast to the northern coasts, which have low coastal types with a wider continental shelf, the Turkish coasts have steep coastal types with a narrow continental shelf. It has a wide continental shelf in the north-western region where large rivers such as the Dnieper, Dniester, and

Danube flow into the sea. Outside of this region, the continental shelf is almost non-existent, and there is only a narrow strip in the west and northwest that is an extension of the continental shelf. The Black Sea's positive freshwater budget (more river/rain inflow than evaporation) is the driving force behind its low surface salinity and the permanent stratification that leads to deep-sea anoxia. The drainage basin includes parts of 24 countries, making riverine inputs a major source of nutrients and pollutants. Annual discharge and drainage area characteristics for the primary rivers contributing freshwater input to the Black Sea are given in Table 1 (Murray et al., 1995; Ozsoy & Unluata, 1997). The three most important rivers that contribute to the Black Sea's volume and terrestrial input are:

I. Danube River: By far the largest contributor, accounting for nearly 50% of the total riverine water discharge. Its flow heavily influences the large North-western Shelf region.

II. Dnieper River: The second-largest in terms of discharge, flowing through Belarus and Ukraine.

III. Dniester River: The third-largest major river, also significantly impacting the North-western Shelf.

Table 1. Annual volume discharge and drainage basin area of the major rivers supplying freshwater and terrestrial input to the Black Sea basin.

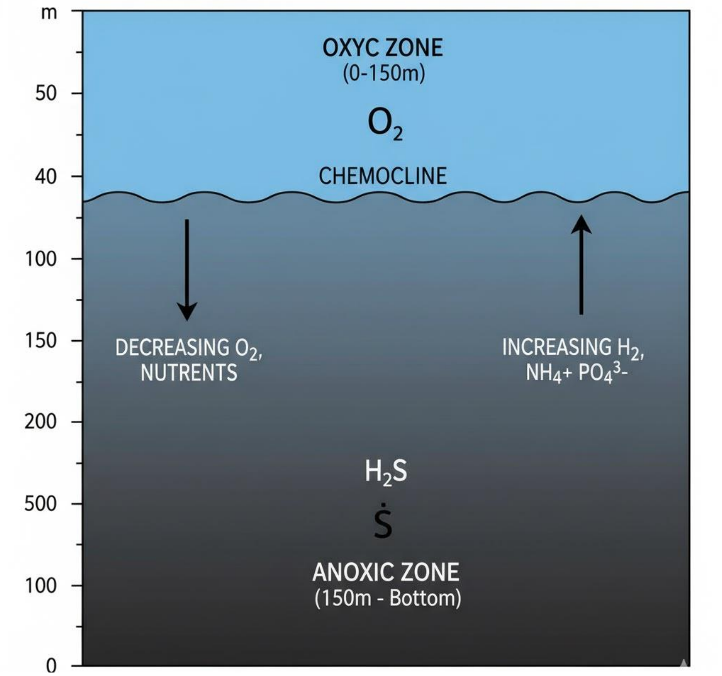
River	*Drainage Area (km^2) (approx)*	*Discharge (km^3/year) (approx)*	*Properties*
Danube	*807000*	*207-210*	*Largest contributor, about 50% of total discharge.*
Dnieper	*504000*	*51.2*	*Second largest contributor*
Dniester	*72100*	*10.2*	*Major impact on the North-Western Shelf.*
Don	*422000*	*29.5*	*Flows into the Sea of Azov, which connects to the Black Sea.*

Hydrochemical Structure of the Black Sea

A unique marine environment, the Black Sea is distinguished by a unique hydrochemical structure that has been the focus of decades of intensive study. The Black Sea contains a confined sea area, with the main inflowing rivers from east to west being the Dniestr, Dnieper, Don, Kuban, and Danube. The Danube is by far the largest in terms of river inflow, accounting for 81% of the total freshwater input. The surface water circulation pattern is characterized by several noteworthy features, especially the large anticyclonic gyre in the interior basin and an essential role for the narrow and shallow Bosporus. The distribution of water properties of the Black Sea shows distinct patterns both horizontally and vertically. The warmer, saltier, and more nutrient-rich surface layer forms from the upper mixed layer in winter productivity; surface ventilation occurs at high latitudes and, occasionally, in the open oceanic region. Waters near the bottom derive mainly from the Mediterranean, consisting of a mixture of the relatively old North Atlantic Deep Water and the younger Levantine Intermediate Water. These waters both mix and are ventilated in the Bosporus, although very little deep water traverses the strait due to a seasonal thermohaline barrier. In response to typical atmospheric forcing such as buoyancy loss and surface stress, vertical processes such as reformation of the pycnocline, double-gyre circulation at the deep level in winter, and deep convection in an open-oceanic region with relatively high latitude and a larger area are frequently observed as a manifestation of different diapycnal mixing regimes. Other important features also stand out with distinct geographic characteristics peculiar to the enclosed basin of the Black Sea (Mee, 1992).

Hydrogen sulphide (H_2S), a poisonous gas that starts to build up at depths of about 200 meters below the surface, is the main characteristic of the Black Sea. A layer of water rich in hydrogen sulphide extends to the seafloor, revealing a highly stratified water column beneath this oxic-anoxic interface in the Black Sea. With an estimated total sulphide pool of 4.6×10^9 tons, the Black Sea is the largest body of water in the world that contains this substance. The Black Sea's general hydrochemical structure, characterized by a strong pycnocline—a sharp density gradient that separates the upper, oxygenated layer from the lower, anoxic layer—is closely associated with the presence of H_2S (Figure 2).

Figure 2. Vertical Black Sea hydrochemical structure



This vertical hydrochemical profile results from a complex interplay between physical, chemical, and biological processes. The inflow of relatively dense, saline Mediterranean waters through the Bosporus Strait creates a strong halocline, which, combined with thermal stratification, leads to the development of the sharp pycnocline. Above the pycnocline, the water column is well-oxygenated due to active exchange with the atmosphere and photosynthetic activity. In addition to its implications for physical oceanography and meteorology, the overall balance of temperature and heat transport makes the Black Sea a critical component of the regional freshwater balance. It is the origin of most of the freshwater in the eastern Mediterranean and plays an active role in the regional freshwater balance of the mid-latitude North Atlantic. Coupled with the last remaining rivers from the eastern European Plain, the Black Sea is clearly the sink of precipitation falling over its basin. Indeed, the Black Sea's importance as a balance also extends to other time and space scales (Humborg et al., 2018)

The distribution of redox-sensitive chemical properties is the defining characteristic of the Black Sea's water column, established by the chemocline (or oxycline), which typically resides between 90 to 150 meters below the surface (Figure 2). This interface separates the oxic (oxygenated) surface waters from the deep, euxinic (anoxic and sulfidic) layer. In the BSW, dissolved Oxygen (O_2) is high (near saturation), while toxic hydrogen sulphide (H_2S) is undetectable, and the pH is high (~ 8.2-8.4). Below the oxycline, in the BDW, O_2 is undetectable, and H_2S concentrations are high (reaching up to 383 µM) and increase with depth. This deep layer is chemically distinct, featuring a lower pH (~7.6-7.7) and the highest total alkalinity (~ 4300 µM) in the entire water column, both driven by the vast microbial process of sulphate reduction that consumes organic matter and generates H_2S. The narrow transition zone between these layers is known as the suboxic zone, characterized by very low O_2 and a temporary, low concentration of H_2S (Volkov & Burlakova, 2012).

Physicochemical Properties of the Black Sea

The Black Sea is distinguished by its complex physicochemical properties, which influence its biological productivity and the distribution of marine species. The most crucial physicochemical properties are salinity, temperature, nutrient levels, oxygen depletion, and stratification. The salinity of the Black Sea varies, with lower salinity near river mouths and higher salinity in deeper layers. The presence of a halocline contributes to the stratification of the water column, impacting nutrient cycling and oxygen distribution. Seasonal temperature variations influence fish spawning and migration patterns. Warmer temperatures can exacerbate the effects of pollution by increasing metabolic rates and altering species interactions. The Black Sea is historically known for its eutrophic conditions, primarily due to nutrient runoff from agriculture and wastewater. This has led to algal blooms, which can deplete oxygen levels and create hypoxic conditions detrimental to marine life. Anoxia, especially in deeper waters, is a critical issue affecting benthic organisms and fish species reliant on oxygen-rich environments (Ozsoy & Unluata, 1997).

The Black Sea is the world's largest euxinic basin (anoxic and sulfidic) and is characterized by strong permanent stratification due to the inflow of low-salinity river water on the surface and high-salinity Mediterranean water at depth via the Bosphorus Strait. This stratification creates two main layers with distinct physicochemical properties: the oxygenated surface layer (Black Sea Surface Water, BSW) and the anoxic, hydrogen sulfide-rich deep layer (Black Sea Deep Water, BDW), separated by a Cold Intermediate Layer (CIL) and a sharp pycnocline/chemocline. Accordingly, the detectable properties vary dramatically between the surface and deep layers of the Black Sea. Table 2 summarizes the significant physicochemical properties.

The nutrient concentrations in the Black Sea Surface Water (BSW) are highly dynamic, exhibiting significant seasonal and spatial variability driven primarily by riverine discharge and biological uptake. Concentrations are notably higher near large river plumes like the Danube Delta and during winter/early spring, when river flow is high and biological consumption is low due to vertical mixing; conversely, they are rapidly depleted in the summer by phytoplankton. Historically, the Black Sea experienced severe eutrophication from the 1970s to the 1990s due to increased inputs of Nitrogen (N) and Phosphorus (P) from rivers. However, current trends show that surface nutrient levels, especially Phosphate (PO_4), have generally declined from their peak periods, a decrease attributed to economic changes and environmental restoration efforts, with concentrations now approaching pre-1970s values in many regions. The vertical distribution of nutrients, which is given in Table 3, is heavily controlled by biological activity and the redox state. The Rim Current, the most active aspect of the sea's circulation and a persistent, cyclonic (counter-clockwise) current system, dominates the hydrodynamic characteristics of the Black Sea's surface waters. Flowing around the entire perimeter of the deep basin along the continental slope isobaths, the Rim Current fundamentally governs the transport of heat, salt, nutrients, and plankton within the upper, oxygenated layer. The main drivers behind this current are thermodynamics/buoyancy, where the substantial freshwater inflow from large rivers like the Danube produces a density gradient that strengthens the cyclonic pattern, and wind stress, which provides Ekman transport. Over the continental slope, the current is narrowest and quickest, frequently reaching speeds of 20–50 cm/s. Its effect extends down to the top of the permanent pycnocline, which is usually ~ 100–200 m deep (Murray & Izdar, 1990; Oguz, Diaconescu & Puzdrowska, 2020).

Table 2. The primary detectable physicochemical properties of the Black Sea.

Property	*Surface Layer (BSW: ~ 0-50 m)*	*Cold Intermediate Layer (CIL: ~50-100 m)*	*Deep Anoxic Layer (BDW: ~ 200 m to bottom)*
Max. Depth (m)	-	-	*2200*
Temperature (^0C)	*~ 8.8-28 (seasonal range)*	*~ 6.5-7.5 (core minimum)*	*~ 8.9-9.1*
Salinity (g/kg)	*~ 17-18*	*~ 18.5-19.5*	*~ 22.0-22.5*
Density (ρ)	*~ 9-14*	*~14-16*	*~17.0-17.3*
Dissolved Oxygen	*High (near saturation)*	*Decreasing/Low*	*Essentially 0*
H_2S	*Undetectable*	*Undetectable*	*~10-383 (increasing with depth)*
Oxic/Anoxic Interface	-	-	*Starts at ~ 90-150 m (Chemocline)*
pH	*~ 8.2-8.4*	*Decreasing*	*~7.6-7.7 (decreasing with depth)*
Total Alkalinity	*~ 3200-3300*	*Increasing*	*~ 4300 (max in bottom layer)*
Nutrients	*Low (consumed by primary production)*	*Maximum concentration (nitracline)*	*Low/Undetectable*

Table 3. The approximate distribution of nutrients vertically in the Black Sea

Nutrient	*Surface Layer (BSW) Nutricline/ Suboxic Zone Deep Anoxic Layer (BDW)*	*Surface Layer (BSW) Nutricline/ Suboxic Zone Deep Anoxic Layer (BDW)*	*Surface Layer (BSW) Nutricline/ Suboxic Zone Deep Anoxic Layer (BDW)*
NO_3^- (µM)	*0.05-0.5*	*~ 4.0-7.0*	*Low/undetectable*
NH_4^+ (µM)	*< 0.5*	*low*	*High, increasing with depth (up to ~ 96.0)*
PO_4^{3-} (µM)	*0.02-0.3*	*Upper and dipper maxima*	*High, increasing with depth (up to ~8.0)*
SiO_4 (µM)	*Variabele (low)*	*increasing*	*High (Released from decaying diatoms)*

Fisheries in the Black Sea

Brief history of fisheries in the Black Sea on Turkish coasts

The history of fishing is older than that of farming (in the form of planting and harvesting), and early fishing methods date back to the earliest periods of human history. Fishing is a form of primary production with methods as ancient as humanity itself (Von Brandt, 1984). In its most fundamental sense, fisheries can be defined as the harvesting and utilization of all aquatic organisms through diverse methodologies. Having persisted since the Upper Palaeolithic era, fishing activities have transitioned from primitive hand-catching techniques to modern mechanized systems integrated with electronic hardware and information technologies. Throughout this evolutionary trajectory, fishing has accrued significant economic value, consequently exerting profound impacts on both the biophysical environment and human societies (Goktürk et al., 2017; Alicli, Gokturk & Deniz, 2018; Ulas, Ozgul & Gokturk, 2024). The history of fishing in Turkish seas extends back to ancient times.

According to known records, commercial fishing has been carried out in the Eastern Black Sea since 2750 BC. During these periods, fishing was conducted using small wooden boats propelled by oars and sails. The primary gear consisted of nets, such as the 'sliding spreaders,' which were woven from cotton yarn and deployed and retrieved solely by human power. A notable early technique, especially for anchovy fishing, involved using light: the nets were cast on moonless nights, targeting anchovies that rose to the surface toward the light of a fan-like lantern held over the sea from the side of the boat. Fishing activities were particularly intense in the Eastern Black Sea region, especially during the Pontus Kingdom period (3rd–1st centuries BC), utilizing primitive methods. For example, pools used for producing bonito fish have survived to the present day. At that time, the coasts of Trabzon, Giresun, Ordu, and Sinop functioned as major fishing markets. Surplus fish were salted and then transported in barrels by ship to the Aegean and Mediterranean countries and large cities like Rome. Dolphin fishing was also practiced along the coasts of Ordu (Perşembe) and Ebulhayr. The oil extracted from these fish was used for both lighting and cooking. Additionally, dolphins and a similar fish called titra were caught along the coasts of Trabzon and Ordu (especially Perşembe) in the Eastern Black Sea. The extracted oil was sent to Istanbul, and the remaining skeletons were used as fertilizer in gardens and fields. The production and external marketing of fish oil from surplus catches were highly important, particularly to the commercial life of Trabzon. Consequently, the fishing and marketing of various seafood products played a significant economic role on these shores until the early 20th century. During the Ottoman period, attempts were made to regulate fishing. The Mussel and Oyster Regulation (1867) was the first legal effort, followed by the Zabıta-i Saydiyye Regulation (1876) and the Istanbul and Surrounding Fish Farm Administration Regulations (1878). However, these early regulations were largely unsuccessful. Following the First World War, fisheries activities became even more primitive. As a result, a series of initiatives were launched during the Republican period to elevate fishing to a systematic, efficient, and economical level (Inonu, 2000; Tureli, Kukner & Dundar, 2007).

Small-Scale Fisheries (SSF) in the Black Sea and Turkish Coasts

Small-scale fisheries (SSF) are a vital, yet often overlooked, component of the Black Sea economy and ecosystem, particularly along the Turkish coast. These fisheries are characterized by the use of small, low-capacity vessels, short trips, and dependence on nearshore resources. They play a crucial role in livelihoods, food security, and coastal culture, despite facing severe environmental and regulatory pressures. Small-scale operations across the Black Sea basin share several common traits:

- Vessels and Gear: SSF typically use vessels under 12 meters in length, employing gear like gillnets, trammel nets, longlines, pots/traps, and beam trawls. These methods are generally selective but can contribute to ghost fishing if lost.
- Target Species: The primary targets are pelagic migratory commercially valuable species in the shallow, oxygenated surface layer, and demersal species, including turbot, whiting, mullets, and various shrimp and crab species.
- Socio-Economic Importance: SSF are employed in rural coastal communities where alternative economic opportunities may be scarce. They supply local markets directly, ensuring fresh, high-quality seafood and supporting traditional dietary habits.

SSF along the Turkish Black Sea Coast represents a vital segment of the national fleet, operating distinctly from the large-scale industrial vessels that primarily target anchovy. Turkish SSF, concentrated along the region that constitutes the largest share of the Black Sea's coastline, are characterized by a dominance of passive gear, heavily relying on gillnets and trammel nets for high-value demersal species like turbot, alongside longlines for Atlantic bonito and traps for crabs. These coastal operations face unique regional pressures, notably intense coastal pressure stemming from rapid urbanization and industrial development, which damages critical nearshore habitats such as spawning grounds and nurseries through construction and pollution runoff (Karakulak & Erdem, 2021; Gokturk, Deniz & Dincer, 2022).

A major impediment to effective management is severe data scarcity, characterized by the lack of robust, disaggregated statistics on the small-scale sector's catch volume, effort, and economic returns, often resulting in its underrepresentation in national policy. Furthermore, Turkish SSF frequently experience significant spatial conflict and competition with industrial trawlers and purse seiners, particularly in the nearshore exclusion zones, which leads directly to gear destruction and the depletion of shared coastal fish stocks (Gokturk et al., 2012; Gokturk & Deniz 2016). Small-scale fisheries are particularly sensitive to the overarching issues of the Black Sea ecosystem:

Overfishing and Stock Depletion: While industrial fleets target pelagic species like anchovy, SSF often target high-value, demersal species like turbot, which have experienced severe stock decline due to intense and often unregulated fishing effort.

Invasive Species: The introduction and spread of invasive species (like the predatory ctenophore *Mnemiopsis leidyi* and, recently, *Beroe ovata*) destabilize the food web, indirectly impacting the productivity of SSF target species.

Climate Change and Pollution: Changes in sea surface temperature and salinity, alongside ongoing chemical pollution (eutrophication and heavy metals), affect the migratory patterns and reproductive success of key commercial stocks, disproportionately impacting the vulnerable nearshore SSF.

Sources of Chemical Pollution

The majority of chemical contaminants enter the Black Sea via two primary pathways: riverine input and atmospheric deposition. Riverine input is the most significant source, carrying pollutants from industrial discharge, urban wastewater, and agricultural runoff across the vast drainage basin encompassing 24 countries. Meanwhile, atmospheric deposition contributes airborne pollutants, such as heavy metals and persistent organic pollutants, which are transported and deposited over the sea's surface. All open basins without a direct connection to the open sea have their own storage and balance systems. Salt, as well as many mineral elements, are collected in basins like the Black Sea with incoming river waters and sea waters, forming due to correct hydrological, physical, chemical, and biological processes. In addition to these natural processes, there is also unwanted pollution in the Black Sea. These pollutants, which are much more unwanted depending on their area, duration, increase-decrease characteristics, source attributes, and adverse effects on life, are found in water, sand, mud, and atmospheric circulation. This pollution is called the external pollution input type. Furthermore, the formation of accidental pollution, which is not counted as unwanted, or the natural substances we use in certain areas and times in some unwanted situations, is called the internal pollution input type. This internal pollution is mainly formed by hydrological, physical, chemical, and biological processes in lake and lagoon types that have been cut off from the open basins without a direct connection to the open sea. Chemical pollutants in the Black Sea can be summarized various sources such as agricultural runoff, industrial discharges, urban wastewater shipping and maritime activities (Tornero & Hanke, 2016:17).

- Agricultural Runoff: The use of fertilizers and pesticides in agricultural practices leads to nutrient loading and the introduction of harmful chemicals into the marine environment.

- Industrial Discharges: Factories along the coast contribute heavy metals and organic pollutants, which accumulate in sediments and enter the food web.
- Urban Wastewater: Inadequately treated sewage contributes to the introduction of pathogens, nutrients, and other pollutants, further degrading water quality.
- Shipping and Maritime Activities: Oil spills and ballast water discharge from ships introduce hydrocarbons and invasive species, impacting local fisheries.

Primary Categories of Chemical Contamination

The Black Sea, a large, deep basin with unique euxinic (anoxic and sulfidic) bottom waters, faces significant environmental challenges due to pervasive chemical pollution. Its nearly landlocked status, coupled with the massive freshwater influx from major European rivers like the Danube, Dnieper, and Dniester, makes it highly vulnerable to pollutants originating across a large, densely populated drainage basin covering nearly one-third of continental Europe Pollutant levels and water quality are closely related to the health of the fish population in the Black Sea. The primary contamination observed in the Black Sea can be summarized as Nutrients (Nitrogen and Phosphorus), heavy metals and persistent organic pollutants (Stan et al., 2014; Alp et al., 2018; Aytan & Mugan, 2020; Boran & Altınok, 2010; Oros et al., 2025).

Nutrients (Nitrogen and Phosphorus)

While essential for life, excess nutrients represent the most historically damaging form of chemical pollution, leading to widespread eutrophication (nutrient over-enrichment). The massive influx of Nitrogen (N) and Phosphorus (P), peaking between the 1970s and 1990s, caused explosive algal blooms. The subsequent sinking and decay of this organic matter consumed vast amounts of oxygen in the intermediate layers, leading to an expansion of the anoxic zone (a phenomenon sometimes called "oxycline shoaling") and causing mass mortalities of demersal fish and bottom fauna.

Due to improved wastewater treatment and economic changes in riparian countries, nutrient levels, particularly Phosphate (PO_4), have significantly decreased from their peak. However, nitrogen inputs remain substantial, maintaining a system prone to nutrient imbalances and localized blooms.

Heavy Metals

The Black Sea receives significant loads of heavy metals from industrial operations (e.g., mining, metallurgy) carried by major rivers. The most common metals detected in the Black Sea such as Mercury (Hg), Cadmium (Cd), Lead (Pb), Copper (Cu), and Zinc (Zn). tend to accumulate in the coastal sediments, particularly in estuarine areas and the deep basin. The anoxic, sulfidic nature of the deep water acts as a sink; most metals react with the abundant H_2S to form highly insoluble metal sulphides (like pyrite, FeS_2), effectively immobilizing them in the deep sediment archive. This immobilization prevents their re-release into the water column under current conditions.

Persistent Organic Pollutants (POPs)

These are toxic, chemically stable compounds that resist environmental degradation and bioaccumulation in the food web e.g. pesticides (e.g., DDT and its residues), polychlorinated biphenyls (PCBs), and polycyclic Aromatic Hydrocarbons (PAHs). POPs are primarily introduced through the atmosphere and river runoff. Due to their lipophilic nature (fat-soluble), they bioaccumulate at high levels in the fatty tissues of marine organisms, posing a risk to top predators (marine mammals and larger fish) and, potentially, to human consumers. Concentrations of these legacy pollutants remain a serious concern despite historical bans on their use.

Table 4. Effect of Major Chemical Pollutants in the Black Sea

Type of Pollutant	*Primary Sources*	*Fate and Transport in the Black Sea*	*Major Environmental Impact*
Nutrients N, P, S	*Agricultural runoff, untreated sewage, industrial wastewater (riverine input).*	*Transported in the upper, oxygenated layer; rapidly cycled on the shelf*	*Eutrophication (nutrient over-enrichment); leads to widespread algal blooms and expansion of the anoxic zone (oxygen depletion).*
Heavy Metals Hg, Cd, Pb, Cu	*Industrial discharge (mining, metallurgy), atmospheric deposition.*	*React with H2S to form insoluble sulphides (e.g., Pyrite) and are effectively sequestered in the deep anoxic sediments.*	*Accumulation in coastal sediments; toxicity and bioaccumulation risk in the food web.*
POPs Pesticides, PCBs, PAHs	*Industrial waste, agricultural application, atmospheric deposition.*	*Highly stable; lipophilic); bioaccumulate up the food chain.*	*Biomagnification in top predators (dolphins, seals, large fish); reproductive and immune system damage in marine mammals.*
Microplastics PE, PP	*Sewage, improper solid waste disposal, maritime activities (riverine input).*	*Float in the surface layer or sink, depending on density and biofouling.*	*Ingestion by plankton and fish; physical damage; potential vector for other chemical contaminants.*

Effect of Chemical Pollution and Contamination on Fisheries

Among the most damaging factors are disruption of reproductive systems, altered food web dynamics, economic consequences, bioaccumulation, and biomagnification. Chemical pollution in the Black Sea poses several critical ecological and economic threats, beginning with the processes of bioaccumulation and biomagnification, where heavy metals and persistent organic pollutants accumulate in fish tissues, creating risks for both aquatic life and human consumers (Figure 3). Furthermore, many pollutants act as endocrine disruptors, causing disruptions to the reproductive systems of fish, which directly translates to reduced reproductive success and subsequent population declines. These chemical stressors also lead to altered food web dynamics by impacting primary producers and zooplankton, thereby disrupting the base of the food chain and profoundly affecting the fish populations that rely on these organisms for sustenance. Collectively, these environmental impacts result in serious economic consequences, as declines in fish populations threaten not only biodiversity but also the local economies reliant on commercial fishing and tourism.

Management and Mitigation Strategies

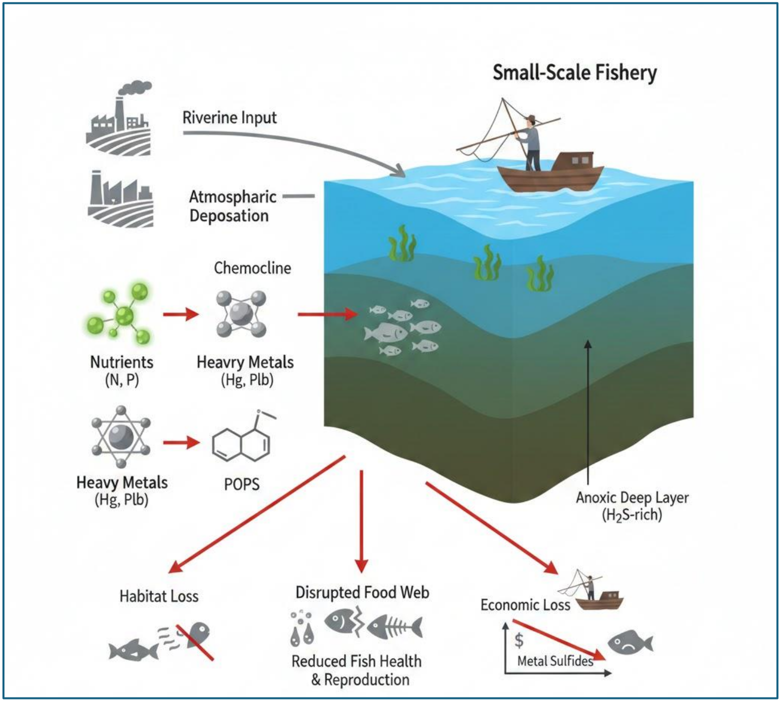
Several case studies illustrate the impact of chemical pollution on specific fish species in the Black Sea (Bat et al., 2017). For instance, studies have shown a decline in anchovy populations linked to hypoxic conditions and increased pollutants. Similarly, the health of sturgeon populations has been compromised due to habitat degradation and chemical exposure. The case studies in the last decades have primarily focused on two major areas related to chemical pollution: Heavy Metals (HMs) and Persistent Organic Pollutants (POPs) accumulation in commercial fish species, and the large-scale ecological impacts of eutrophication (nutrient pollution) on fish habitats. Studies, particularly along the Turkish and Romanian coasts, often assess human health risk alongside ecological impact.

Table 5. Impact of Chemical Pollution on Black Sea Fisheries (Last Decades)

Type of pollution	*Reported Species*	*Observed Impacts on Fisheries* *Region & Timeframe* *Reference Focus*
Nutrients (N & P)	*Anchovy* *Turbot* *Sprat*	*Habitat Loss: Eutrophication-induced O_2 depletion expands the suboxic/anoxic zone, severely limiting the living space for demersal species and forcing pelagic fish into a shallower layer.* *Food Web Disruption: Changes in phytoplankton dominance (shift from diatoms) impacting the food base for species like anchovies.* *Basin-wide (1980s-2000s)* *Ecological/Ecosystem-scale*
Heavy Metals	*Red Mullet, Whiting, Turbot, Sprat, Anchovy, Horse Mackerel*	*Bioaccumulation: High levels of Pb,Cd, Hg and Ni detected in muscle and liver tissues (e.g., higher Ni in some Turkish studies). Physiological/Sub-lethal Effects: Potential for oxidative stress, toxicity, and disruption of enzymes in fish.* *Human Health Risk: Most studies conclude risk from consumption is currently low (below regulatory limits), but continuous monitoring is essential, particularly near pollution hotspots.* *Turkish, Romanian, and Bulgarian Coasts (1990s-Present)* *Ecotoxicology/Human Health*
Microplastics	*Anchovy, Horse Mackerel, Bonito, Garfish, Bluefish, Red Mullet, Whiting*	*Ingestion: High prevalence of microplastics (mostly fibers) found in the gastrointestinal tracts of all commercial fish species analyzed, with the highest rates in Bonito.* *Chemical Transfer: Potential for microplastics to transfer adsorbed chemical contaminants to fish tissues.* *Basin-wide, particularly Turkish & Romanian Coasts (2010s-Present)* *Ecological/Bioaccumulation*
POPs , PCBs, PAHs, Pesticides	*Seals and Dolphins, Large Pelagic Fish*	*Biomagnification: Accumulation of lipophilic contaminants in fatty tissues.* *Endocrine/Reproductive Effects: High levels linked to impacts on immune systems and reproductive success in marine mammals, indicating a general health stressor across the food web.* *Basin-wide, inferred from high trophic level studies (1990s-Present)* *Ecotoxicology/Food Web Transfer*

Addressing chemical pollution in the Black Sea requires a multifaceted approach through coordinated efforts at local, national, and international levels. Central to this strategy is the strengthening of regulatory frameworks to govern agricultural practices and industrial discharges, thereby minimizing harmful runoff and point-source pollution. These legal measures must be supported by comprehensive monitoring programs designed to track water quality and fish health, allowing for the identification of pollution hotspots and the objective assessment of management efficacy. Furthermore, fostering community engagement is essential; by involving local stakeholders in conservation initiatives and promoting sustainable fishing practices, the pressure on vulnerable fish stocks can be effectively alleviated. Ultimately, the integration of these diverse strategies is paramount to ensuring the long-term ecological resilience and economic viability of the Black Sea’s marine resources.

Figure 3. Impacts of chemical pollution on the Black Sea SSF



Conclusion

The chemical pollution in the Black Sea carries several critical implications for both its ecosystem and human health. A primary ecological consequence is habitat loss, where the expansion of the suboxic and anoxic zones has severely compressed the usable habitat for commercial fish species, thereby intensifying fishing pressure on the limited oxygenated surface layer. Furthermore, the transfer of Persistent Organic Pollutants (POPs) through the food web leads to biomagnification, resulting in elevated contaminant concentrations in top predators like seals, dolphins, and large pelagic fish, which in turn negatively affects their reproductive success and immune systems. Finally, there is a direct coastal risk, as estuaries and coastal zones, particularly near major ports (e.g., Odessa, Constanta, Varna), exhibit the highest contamination levels, posing direct dangers to human health through the consumption of contaminated seafood and exposure to polluted bathing waters. In summary, while significant efforts have successfully reduced the catastrophic level of eutrophication seen in past decades, the Black Sea continues to face threats from a complex mix of legacy and modern chemical pollutants that challenge its unique biogeochemistry and the overall health of its ecosystem.

The Black Sea’s fisheries are under threat from chemical pollution, which affects not only the marine ecosystem but also the socioeconomic fabric of the surrounding communities. Understanding the physicochemical properties of the Black Sea and the sources and impacts of pollution is crucial for developing effective management strategies. Collaborative efforts are needed to restore the health of this vital marine resource and ensure its sustainability for future generations. Effective management requires integrating SSF into participatory decision-making processes, improving monitoring of coastal stocks, and implementing co-management schemes that respect local knowledge and traditions to ensure long-term sustainability. In summary, strategies for reducing marine pollution in the Black Sea can be categorized as follows:

Policy Interventions: Governments must tighten regulations on industrial discharges and agricultural runoff to minimize the influx of nutrient pollutants into the marine environment.

Community Engagement: Involving local fishing communities in monitoring and conservation initiatives can enhance the sustainability of fish production. Furthermore, education and awareness campaigns can serve to strengthen these conservation efforts.

Waste Management and Plastic Mitigation: Implementing robust waste management strategies and limiting plastic consumption are critical to protecting marine life and reducing plastic pollution.

Research and Monitoring: Continuous surveillance of marine pollution and its impacts can provide decision-makers and communities with timely data, thereby facilitating more effective interventions.

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CHAPTER 5

WINTER HERBAL TEAS, THEIR PHYTOCHEMICALS, AND BIOCHEMICAL-PHYSIOLOGICAL EFFECTS

ZEYNEB KARAKUŞ[1]

Introduction

Winter is a time when the days get shorter and the air becomes noticeably colder. As a result, people tend to move less and sweat less, and the detoxification processes that depend on physical activity and perspiration slow down. In such conditions, the delicate balance between free radicals, which can damage tissues, and antioxidants, which neutralize these molecules, may be disturbed. This imbalance can trigger oxidative stress and weaken the immune system (Dündar & Aslan, 2000; Pal, 1994; Thomas, 1995). One simple and widely used way to benefit from antioxidant plants and to help maintain physiological homeostasis is to consume them in the form of herbal teas (Dündar, 2001; Evcimen & Aslan, 2015).

In countries with a Mediterranean climate, people often drink teas prepared from medicinal and aromatic plants such as ginger, mint, cinnamon, lemongrass, lemon balm, echinacea, sage,

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mountain tea (*Sideritis* spp.), chamomile, blackberry, raspberry, cranberry, rosehip, St. John's wort and elderberry. Teas made from fruits like orange, grapefruit, carrot, apricot, peach, red plum and blueberry are also common. These drinks are preferred especially during the winter months and have been used for centuries within folkloric traditions and traditional healing practices.

Interestingly, although many of these herbal and fruit teas are well known, the potential of black and green tea to support winter metabolism and contribute to vitality is still not fully appreciated. Tea is actually an excellent winter beverage because it contains high amounts of antioxidant polyphenols-particularly flavonols (catechins), flavonol glycosides and gallate-type tannins-as well as enzymes, alkaloids, nitrogenous substances, pectic compounds, vitamins, minerals and volatile components (Dündar, 2001; Evcimen & Aslan, 2015). For this reason, black, green and white teas obtained from *Camellia sinensis* should be regarded as leading winter tea options (Dündar, 2001).

Grape tea is another drink worth promoting. Thanks to its polyphenols, anthocyanins, carotenoids, resveratrol, quercetin and ellagic acid, it offers a rich phytochemical profile (Craig, 1997; Dündar, 2001). In this chapter, teas prepared from such medicinal and aromatic plants are considered as functional phytotherapeutic products that support adaptation to winter conditions and help protect against cellular injury and disease (Evcimen & Aslan, 2015). The focus is on the roles and effects of the phytochemicals present in these teas (Craig, 1997).

Phytotherapy, literally "treatment with plants", has a very long history, although the term itself was introduced into the medical literature only about eighty years ago by the French physician Henri Lenclerc in the journal *La Presse Médicale*. In phytotherapy, chemical compounds found naturally in plants are used as medicines without first being isolated (Aslan, 2016). Many plants around us act as physiological allies: some relieve stress and anxiety, some calm the stomach, others stimulate intestinal movements or reduce gas (Aslan, 2016).

Human beings have used plants to maintain homeostasis and treat disease since ancient times. Vegetables, grains, legumes and many plant parts-fruits, leaves, stems and roots-contain thousands of different chemicals that help keep internal balance and support vitality (Craig, 1997). Owing to these features, plants and their phytochemicals are now seen as powerful tools for defence, especially for their antioxidant actions against major health problems such as cancer, cardiovascular disease, hormonal disorders and diabetes (Craig, 1997; Dündar & Aslan, 2000). At the same time, scientific reports have pointed out that not every antioxidant is safe under all circumstances. This has encouraged researchers to identify safer antioxidant plants and plant-based products and has led to a reconsideration of habits related to the use of antioxidant herbal teas (Thomas, 1995).

Among the various ways of using plants for health and well-being-besides extracts or purified phytochemicals employed as pharmaceutical raw materials-the most common is simply drinking herbal teas (Aslan, 2016). Within this group, teas produced from *Camellia sinensis* (black, green and white tea) occupy a central position (Dündar, 2001). Their physiological effects and their contribution to vitality are now being described in much greater detail than in the past (Dündar, 2001; Evcimen & Aslan, 2015).

When days grow shorter and temperatures fall, the body’s chance to benefit from detoxification mechanisms linked to movement and sweating diminishes. For this reason, it is useful to prepare for winter on both a psychological and physiological level. Such preparation involves strengthening the immune system, keeping stress at a manageable level and supporting the body with adequate iron, carotenoids, vitamin D and probiotics. Vitamin C, omega fatty acids and a number of traditional or modern herbal supplements are also frequently recommended as part of this strategy (Müftüoğlu, 2012; Müftüoğlu, 2018).

Winter typically brings dull, sunless skies and cold, rainy, foggy or snowy weather. Long and chilly nights influence not only the body but also the mind. Feelings of uneasiness, low mood or emotional tightness can become more noticeable. A psychological state often seen in this season is known as Seasonal Affective Disorder (SAD) (Aslan, 2017; Çevik & Aslan, 2015). Unlike a brief episode of boredom, SAD can affect an individual for days at a time. In addition to sadness, tiredness and lack of energy, it may include depressive symptoms such as changes in appetite, intense cravings for particular foods, weight gain and an excessive desire to sleep (Çevik & Aslan, 2015). In this sense, it is a form of seasonal depression commonly referred to as "winter depression" (Çevik & Aslan, 2015).

Winter depression is thought to be associated with altered levels of serotonin and melatonin-hormones strongly influenced by reduced daylight and other seasonal factors-and is considered a reflection of changes in endocrine and neuronal systems (Çevik & Aslan, 2015). Genetic predisposition, long-lasting periods of stress and disturbances in body biochemistry also appear to contribute (Çevik & Aslan, 2015). People therefore tend to seek sunlight more in winter; this behaviour can be regarded as a kind of self-directed phototherapy. Eating habits also shift with the seasons (Çevik & Aslan, 2015).

A strong immune system is especially important at the entrance to winter. To this end, many individuals use herbal products such as ginger and echinacea, beta-glucan-containing preparations, zinc, vitamin C and N-acetylcysteine. These are not always part of daily life in other seasons but are taken to support immune physiology against influenza, the common cold, asthma and pneumonia attacks, fever, sneezing and cough (Müftüoğlu, 2018). Preparations from Umckaloabo (*Pelargonium sidoides*), a plant native to Africa, have also become popular, as studies suggest that it can activate immune and defence cells against viruses causing upper respiratory and lung infections (Müftüoğlu, 2018).

For a metabolism that copes well with winter, foods such as beans, chickpeas, lentils, citrus fruits and green leafy vegetables are important sources of iron, potassium, plant proteins, folic acid, B-group vitamins and vitamin C (Müftüoğlu, 2012). Grapefruit may boost metabolic rate and enhance resistance; red grapes provide fibre, vitamins, minerals and diverse phytochemicals; pomegranate offers strong antioxidant activity and can help regulate endocrine function; and broccoli contributes with its enzyme and vitamin content (Müftüoğlu, 2012; Dündar, 2001). Together, these foods give substantial support to the immune system (Müftüoğlu, 2012).

Chestnut, an endemic resource for Türkiye, can also be considered a valuable medicinal food in winter, as long as its starch content is taken into account. It supplies protein, fibre, potassium, phosphorus, calcium and B-group vitamins (Müftüoğlu, 2012). Nuts and seeds-almonds, pistachios, hazelnuts, walnuts, pumpkin seeds and sunflower seeds-as well as fish such as anchovy, mackerel, bluefish and bonito are rich in omega-3 and omega-6 fatty acids, calcium, vitamin E and arginine, a key precursor for nitric oxide (Müftüoğlu, 2012). It has been reported that eating about 30 g of nuts per day may lower the risk of sudden death by 20%, the risk of heart attack by 30% and the risk of cancer by roughly 10% (Müftüoğlu, 2012).

For people of all ages who wish to adapt their physiology to winter, simple drinks can also play a role. Young, adult and elderly individuals may prefer water or ayran, whereas children are often encouraged to drink milk. Goat milk, which tends to cause fewer allergic reactions and contains relatively more protein, vitamins and minerals, may be chosen in some cases, but for newborns breast milk remains irreplaceable in any season, including winter (Müftüoğlu, 2016).

Vegetable soups, coffee and salep are not usually counted among herbal teas, yet they can be considered appropriate hot beverages for cold weather. Pumpkin soup, cabbage soup and mixed vegetable soups are low in calories but rich in nutrients and therefore deserve a place in meals designed to support winter metabolism (Müftüoğlu, 2012). Tomato, a notable source of lycopene; pumpkin, which is rich in carotenoids; and cabbage, with its strong antioxidant character, give rise to soups that may be regarded as medicinal plant-based foods that support the immune system (Dündar, 2001).

Aerobic life, which depends on oxygen, inevitably generates reactive oxygen and nitrogen metabolites known as free radicals. These molecules are natural products of aerobic metabolism (Pal, 1994; Dündar & Aslan, 2000). Increased viral and bacterial challenges lead to heightened phagocytic activity, and air pollution, cold air and fog further contribute to the production of reactive species; under these circumstances it becomes harder for the organism to maintain internal balance (Dündar & Aslan, 2000; Pal, 1994).

It is well established that oxidative products and the reactions they undergo can damage tissues, generate toxic intermediates and promote pathological changes. In this way they pose a serious threat to physiological vigour, immune resistance and homeostatic stability (Thomas, 1995; Dündar & Aslan, 2000). Virtually all cellular components are potential targets for free radical attack, oxidation and peroxidation reactions. Proteins and genetic material are particularly prone to oxidation, whereas phospholipids form an ideal environment for lipid peroxidation (Mead, 1989; Thomas, 1995).

Oxidation and peroxidation reactions enhanced by seasonal factors can denature proteins, inactivate enzymes, cause hydroxylation and mutations in nucleic acids, disrupt cross-links, weaken tissue integrity and eventually result in cell death (Mead, 1989; Thomas, 1995). Herbal teas prepared from aromatic medicinal plants can provide additional extracellular antioxidant support to the body’s own defences, which are carried out by antioxidant enzymes within cells and by various macromolecules in the extracellular space (Dündar & Aslan, 2000; Pal, 1994).

Some Medicinal Aromatic Plant in Tea Form

In winter, overall fluid intake and water turnover tend to decline. Under these conditions, herbal teas serve not only as pleasant warm drinks but also as reliable sources of liquid (Müftüoğlu, 2012). Their use has attracted the attention of researchers in medicine, veterinary science, biology and pharmacy. Because they are inexpensive, widely preferred and associated with beneficial effects, herbal teas have progressed to the stage of being evaluated for inclusion in the Turkish Pharmacopoeia (Aslan, 2016).

Many different teas have been studied in this context… The available studies indicate that these teas can act as effective beverages and phytotherapeutic materials that support physiological homeostasis and promote a sense of vitality (Dündar, 2001; Evcimen & Aslan, 2015).

Phytochemicals in Herbal Teas and Their Physiological Effects

As awareness of antioxidant safety has grown, interest in medicinal and aromatic herbal teas has also increased. Diets that are rich in vegetables, fruits, grains, cereals and legumes are thought to help reduce the likelihood of cardiovascular disease, hypertension, cancer and diabetes (Craig, 1997). Plants owe much of this protective potential to their antioxidant compounds, which defend cells against the damaging consequences of oxidative reactions (Craig, 1997; Dündar & Aslan, 2000). Consequently, the use of medicinal plants is steadily expanding (Aslan, 2016).

Modern analytical methods have revealed tens of thousands of phytochemicals in plants, and their biological effects are being investigated one by one (Craig, 1997; Dündar, 2001). … These include catechins, isoflavans, indoles, carotenoids, anthocyanidins, ellagic acid, polyphenols, phenolic compounds, flavonoids, isoflavones, coumarins, lignins, lactones, saponins, glucosinolates, phytosterols, phytoestrogens, terpenes and quercetin (Craig, 1997; Dündar, 2001).

Isoflavans

Licorice root, hops, green tea, dry beans, other legumes and soybeans are notable sources of isoflavones and related compounds. Isoflavans have been reported to repair cells damaged by oxidative processes, inhibit LDL oxidation and thereby protect cells from oxidative injury, and influence the metabolic profile of steroids and various cytochrome P450 substrates (Craig, 1997; Dündar & Aslan, 2000).

Ellagic acid

Ellagic acid is a strong antioxidant that may protect DNA against damage caused by polluted air, cigarette smoke and combustion products, prevent degradation of the tumour-suppressor gene *p53* by cancer cells and bind carcinogenic molecules, rendering them inactive (Craig, 1997; Dündar, 2001). Walnuts, grapes, pomegranates, blackberries, cranberries, raspberries, cherries, apples, strawberries and turmeric are rich dietary sources, with raspberries being especially notable (Craig, 1997).

Gallic acid

Gallic acid occurs widely in plants, and its most effective derivatives are tannins. Historically, polyphenols in tea rich in gallic acid were simply referred to as tannins. Important sources include tea leaves, plant galls, grapes, hops and oak bark. Gallic acid has well-documented antioxidant, antifungal and antiviral properties (Dündar & Aslan, 2000; Thomas, 1995).

Phytates (phytic acid)

Phytates contribute to the regulation of iron absorption and thus help prevent oxidative stress. They are present in flaxseed, legumes, seeds, grains and various other plant seeds (Craig, 1997).

Indoles

Indole compounds participate in neural transmission and synaptic activity, help regulate blood glucose levels, lower blood pressure and support the formation and release of beneficial estrogen subgroups. Broccoli, kale, Brussels sprouts, cabbage, cauliflower, turnip greens, mustard greens, ginseng, sesame, bitter melon, bottle gourd and many leafy vegetables provide appreciable amounts of indoles (Craig, 1997; Dündar, 2001).

Flavonoids

Flavonoids, often discussed together with catechins, are among the best-studied antioxidant molecules. Tea and many berries are particularly rich in these compounds, and green tea generally contains more catechins than black tea. Flavonoids suppress inflammatory responses, inhibit microsomal peroxidation reactions, modulate cell proliferation and influence the cardiac conduction system (Craig, 1997; Dündar & Aslan, 2000; Evcimen & Aslan, 2015).

Terpenes

Terpenes help prevent microsomal lipid peroxidation and reduce oxidative stress in cells. Citrus fruits, cherries and sour cherries are among the major dietary sources (Craig, 1997).

Phenolic acids

Phenolic acids occur abundantly in vegetables, walnuts, hazelnuts, cherries, apples, strawberries, raspberries, broccoli, oranges and tomatoes. Reported effects include modulation of enzymatic activities, inhibition of nitrosamine formation and improvement of disturbances in plasma lipid profiles (Craig, 1997; Thomas, 1995).

Coumarins

Coumarins may be toxic at high intakes. They are present in lavender, licorice root, cinnamon, celery seed, blackberry, apricot and cherry. Some coumarins protect DNA from harmful agents, while furocoumarins such as isoimperatorin and bergapten inhibit acetylcholinesterase and butyrylcholinesterase, enzymes responsible for acetylcholine breakdown (Craig, 1997).

Polyphenols

Polyphenols provide cellular protection primarily through inhibition of LDL oxidation. Hops, olives, black and green tea and many grape varieties are rich sources. Classical black tea contains large amounts of antioxidant polyphenols, and the protective effect of olive oil in oxidative-stress-related diseases has been attributed to its polyphenol content (Craig, 1997; Dündar & Aslan, 2000).

Lycopenes

Lycopene and related carotenoids show antioxidant and anticancer activity and may help regulate male sex hormone levels. They are responsible for the red colour of certain fruits and vegetables. Although watermelon and grapefruit contain lycopene, ripe tomatoes are considered the richest dietary source (Craig, 1997).

Glycyrrhizin

Glycyrrhizin, best known from licorice root, helps prevent DNA damage, neutralize toxic catabolic products, provide antiviral action and contribute to antioxidant defence systems (Craig, 1997; Dündar & Aslan, 2000).

Isothiocyanates

Isothiocyanates protect DNA by stimulating detoxification enzymes, inhibit cancer cell growth and induce apoptosis by modulating cellular signalling pathways. Watercress, radish, cabbage varieties, cauliflower, broccoli, rapeseed and mustard are major dietary sources (Önsesik & Acar, 2003).

Anthocyanins and anthocyanidins

These pigments are responsible for red, purple and bluish colours in plants and act as powerful antioxidants. They are associated with protection against cancer and atherosclerosis and are abundant in berries, grapes, cherries, pomegranates, red cabbage and many coloured fruits and vegetables (Craig, 1997; Dündar, 2001).

Carotenoids

Carotenoids help repair oxidative damage, prevent DNA strand breaks and may contribute to cancer prevention. Endive, fennel, pineapple, kiwi, tomato, carrot, spinach, cauliflower, grapes and celery are notable sources (Craig, 1997).

Sulfites

Sulfite-containing compounds increase the activity of detoxification enzymes such as glutathione transferase and quinone reductase, aiding in the elimination of toxic chemicals and metabolites. They occur in garlic, onions, chives, leeks, pineapple and broccoli (Craig, 1997).

Quercetin

Quercetin is a potent flavonoid antioxidant found in grape seeds and many fruits and vegetables. It counteracts free radical damage and plays a role in ageing and inflammation-related processes (Craig, 1997; Dündar & Aslan, 2000). Red onions are among the richest sources; average daily intake is estimated at 10–100 mg. Clinical observations during the COVID-19 pandemic indicated antiviral and anti-inflammatory effects, particularly when combined with vitamin C (Craig, 1997; Müftüoğlu, 2018).

Resveratrol

Resveratrol is a strong natural antioxidant present in grapes, grape leaves, molasses and grape juice and is widely studied for its protective metabolic and cardiovascular effects (Craig, 1997; Dündar, 2001).

Sulforaphane

Sulforaphane is regarded as one of the most powerful anticancer phytochemicals identified to date. Cabbage, kale, cauliflower and radish are its principal dietary sources (Craig, 1997; Önsesik & Acar, 2003).

Capsaicin

Capsaicin, responsible for the pungency of chilli peppers, accelerates metabolism, lowers cholesterol levels and dampens inflammatory processes. Experimental studies also suggest inhibition of nitrosamine formation (Craig, 1997).

Pectin

Pectin is a soluble fibre with cholesterol-lowering effects and is found in high amounts in apples and grapefruit (Craig, 1997).

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CHAPTER 6

Aromatic Compounds Used as Organic Fertilizers

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Tülay DiziKISA[2]

1. Introduction

Organic fertilizers are considered as "natural materials that provide nutrients to the plant for a long time"; compost, farm manure, green manure and organic waste-based inputs were evaluated in this context. However, the current approach; defines organic fertilizers not only as macro and microelement resources, but also as chemical and biological regulators that affect the amount of soil organic matter, microbial ecology and plant metabolism (Stevenson, 1994; Canellas & Olivares, 2014). Many biological and ecological effects observed in organic fertilizer applications are important for the transformation of organic materials, as they occur through aromatic components of organic matter (e.g., humic substances, phenolic acids, and aromatic carbon structures) (Stevenson, 1994; Lehmann & Joseph, 2015).

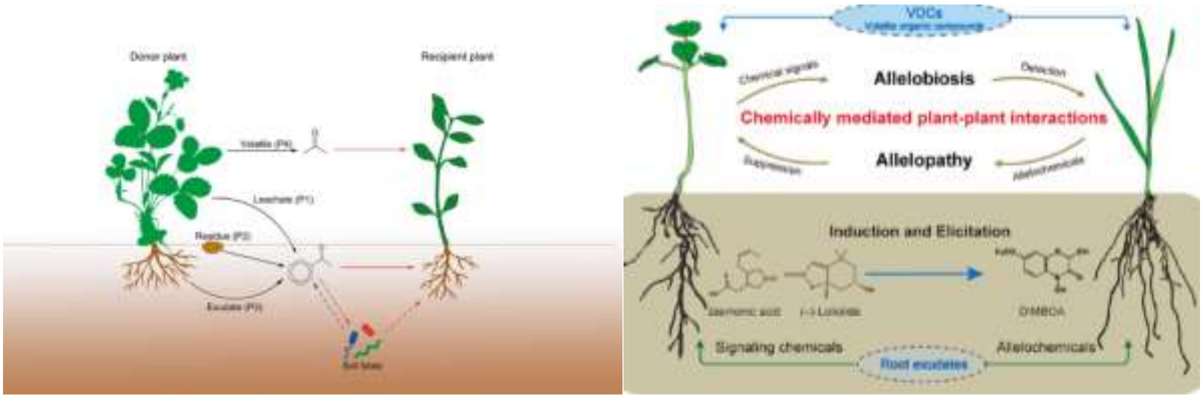

Figure 1. Schematic representation of chemical interactions between plants

Importance of aromatic compounds for organic fertilizers:

1. Stability and buffering in soil: The delocalized π-electron system of aromatic structures imparts high chemical stability to these compounds. In this way, aromatic components (especially humic acid, fulvic acid and characterization of biochar aromatic carbon) can remain in the soil longer and contribute to processes such as nutrient retention and release, pH buffering and organic matter stabilization (Stevenson, 1994; Lehmann & Joseph, 2015).

2. Microbiota and rhizosphere regulation: Phenolic acids and similar low molecular weight aromatic organic compounds can be used as "carbon source/signal" molecules for

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microorganisms; however, they can also cause suppressive effects depending on concentration and environmental conditions. Therefore, the same compounds can alter rhizosphere microbial composition depending on dose and environment, and this change can lead to knock-on effects on plant health and quality (Blum, 1996; Bao et al., 2022).

3. Determinants of Chemical Quality in Medicinal Plants: The pharmacological value of medicinal plants is often related to phenolics, flavonoids, and other secondary metabolites of aromatic origin. The indirect regulation of secondary metabolite biosynthesis by affecting root formation and nutrient uptake dynamics through signal transduction mechanisms due to abiotic and biotic stresses of aromatic components of organic fertilizers establishes an interdisciplinary connection between agricultural sciences and pharmacy based on chemical quality. Humic substances can change root formation and thus increase nutrient intake; it has also been reported that a relationship can be established between the structural composition of humic substances, especially aromatic components, and biological activity (Canellas & Olivares, 2014; Nardi et al., 2021).

At this point, the main expectation from the pharmacy perspective is that the herbal raw material shows a consistent chemical profile. This suggests that organic fertilizer applications should be traceable, controlled and standardized, not random. WHO's GACP approach and EMA's current GACP guideline support this holistic view to ensure quality in the production, collection and primary processing processes of medicinal plants (WHO, 2003; EMA, 2025).

2. Chemical Properties of Aromatic Compounds

2.1. Aromatic structure, reactivity and interaction mechanisms in soil

Aromatic compounds are organic molecules that contain benzene ring or aromatic ring systems and are stable due to the delocalization of π-electrons. This determination leads to two important outcomes:

Tendency to adsorption to soil colloids: Compounds containing aromatic rings can bind more strongly to organic matter fractions and some mineral surfaces. This affects the bioavailability and persistence of the compound (Stevenson, 1994).

Dependence of transformation on microbial processes: Many aromatic compounds are broken down or transformed in soil, primarily through microbial enzymatic processes. Therefore, environmental factors such as temperature, humidity, pH, and microbial community composition play a decisive role in the stability and content of aromatic compounds (Bao et al., 2022). Reviews showing that phenolic acids can alter microorganism communities in the rhizosphere and are sometimes associated with negative feedbacks such as soil fatigue or monoculture cultivation emphasize that aromatic compounds are not only beneficial in soil, but also a class of chemicals that can cause problems if the correct dose and binding are not provided (Blum, 1996; Bao et al., 2022).

2.2. Major classes of aromatic compounds in organic fertilizers

(A) Humic substances (humic acid, fulvic acid, humin)

Humic substances are complex organic fractions that derive from decomposing biomass and carry functional groups (carboxyl, phenolic OH, etc.). The classical humus chemistry literature deals in detail with the formation, fractionation, and reactivity of humic substances (Stevenson, 1994).

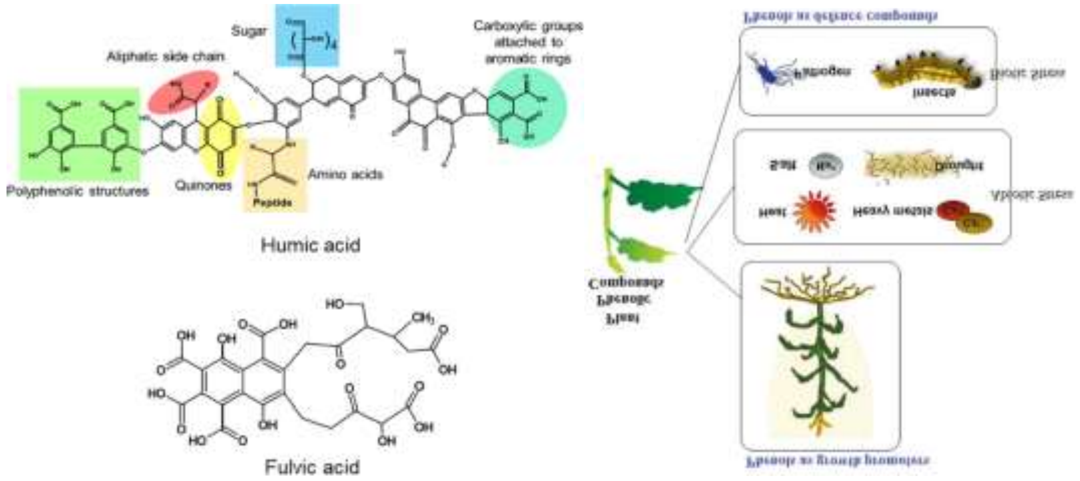

Figure 2. Schematic representation of the aromatic structures of humic and fulvic acids and their effects on nutrient dynamics and plant root development in soil.

The importance of aromatic components in humic substances comes from:

- ✓ Chelating and complexation: Carboxyl and phenolic groups attached to the aromatic structure can be complexed with microelements such as Fe, Zn and Mn. As a result, the nutrient uptake of the plant is indirectly affected (Marschner, 2012).
- ✓ Root formation and physiology: There are comprehensive evaluations that humic substances can affect plant growth, especially through root formation; an increase in root surface area can strengthen nutrient uptake (Canellas & Olivares, 2014).

In addition, a more recent review discusses the relationship between chemical structure and biological activity of humic substances, and in some studies, a relationship can be established between lignin-based aromatic components and root growth stimulation; in some other studies, it is stated that simple phenolics may be active components (Nardi et al., 2021).

It should be noted that there are different opinions in the literature on the structure of humic substances and the mechanism of humification. Therefore, instead of a single structure model, it is considered more reliable to use operational definitions such as functional group richness and aromatic/aliphatic component ratio. This approach aligns with Stevenson's classical framework (Stevenson, 1994).

B) Phenolic acids and simple aromatics

Phenolic acids, such as ferulic acid, p-coumaric acid, and vanillic acid, are aromatic compounds that are released in plant residues and composting processes and play an active role in the rhizosphere. The "low dose stimulation, high dose suppression" character of these compounds (allelopathic effect) has been discussed in the literature for a long time (Rice, 1984; Blum, 1996).

As an important nuance, it is noted that in some studies of allelopathic phenolic acids, the concentrations measured under field conditions may be lower than laboratory inhibition levels. Thus, the action of these compounds may occur indirectly through microbial transformation and rhizosphere processes rather than direct toxicity (Blum, 1996).

C) Biochar and aromatic carbon structures

Biochar is a material formed as a result of the pyrolysis of biomass under limited oxygen conditions and is generally rich in aromatic carbon. When applied to soil, it can affect the persistence of organic matter, water retention properties, and some nutrient dynamics. One of the primary sources of biochar literature is the comprehensive work edited by Lehmann and Joseph (Lehmann & Joseph, 2015).

Biochar often does not directly provide high N:P:K; however, adsorption capacity can indirectly affect nutrient efficiency and plant performance through microhabitat creation and improving soil physico-chemical properties (Lehmann & Joseph, 2015).

2.3. Chemical logic explaining the "fertilizer effect" of aromatic components

It is useful to think about the contribution of aromatic compounds in the fertilizer system in terms of the following three chemical axes, rather than "direct nutrient provision":

Functional group chemistry (–COOH, –OH, carbonyl, etc.)

Complexation/chelation and ion exchange can increase the availability of nutrients for the plant. The growth-promoting effects of humic substances are discussed within this framework (Canellas & Olivares, 2014; Nardi et al., 2021).

Degree of aromatic structure and persistence

As aromatic carbon increases (especially in biochar), persistence may increase. In this case, it promotes long-term soil improvement (Lehmann & Joseph, 2015).

Mechanisms of signal transduction and microbial feedback in the rhizosphere

Compounds such as phenolic acids can alter the microbiota; this may indirectly direct the secondary metabolite profile by affecting the plant's nutrient uptake and stress response (Blum, 1996; Bao et al., 2022).

3. Sources of Aromatic Compounds in Organic Fertilizer Systems

3.1. Vegetable Residues and Lignin-Based Aromatic Compounds

Figure. 3. Spectroscopic determination of phenolic compounds in organic fertilizers and schematic representation of basic phenolic structures of lignin origin.

The most important source of aromatic compounds in organic fertilizer systems is vegetable residues. Leaf, stem, root and bark tissues remaining after harvest; Structurally, it is rich in lignin, cellulose, and hemicellulose. Among these components, lignin, in particular, plays a central role in the chemical foundation of organic fertilizer systems due to its composition of phenylpropanoid units containing aromatic rings.

During the microbial and enzymatic breakdown of lignin:

- ✓ Ferulic acid,
- ✓ Cinnamic acid,
- ✓ Vanillic acid,
- ✓ p-Coumaric acid

low molecular weight aromatic compounds such as are released. These compounds accumulate temporarily during the composting process and then contribute to the formation of humic substances (Stevenson, 1994; Lehmann & Joseph, 2015).

This process shows that aromatic compounds in organic fertilizers have a dynamic structure; that is, they vary depending on the degree of decomposition and the time of application rather than a fixed content.

3.2. Aromatic Compound Profile in Compost and Green Manures

Compost and green manure applications ensure that aromatic compounds are introduced into the soil in a controlled manner in organic fertilizer systems. Along with the humification of organic matter during composting:

- Aromatic carbon ratio increases,
- Phenolic and carboxylic functional groups are enriched,
- Chemical stability increases.

Especially in well-matured composts, the amount of free phenolic acids that can have a phytotoxic effect decreases; humic-like aromatic structures become dominant. This makes compost both plant-friendly and a long-term effective organic fertilizer (Canellas & Olivares, 2014).

In green manure applications, fresh plant biomass mixed into the soil may cause an increase in phenolic acid concentrations in the short term. Although this increase has an allelopathic effect in some cases, it can promote secondary metabolite biosynthesis by creating mild stress signaling in plants when managed appropriately (Rice, 1984; Blum, 1996).

3.3. Aromatic Plant Residues: A Special Resource Group

Aromatic plants (e.g. thyme, rosemary, sage, fennel) leave residues rich in phenolics, aromatic aldehydes and terpene-aromatic hybrid structures after agricultural production. The use of these residues as compost or soil amendment produces a different chemical impact profile than conventional vegetable waste.

The prominent features of using aromatic plant residues as organic fertilizer are as follows:

- Creating selective pressure on the soil microbiota,
- Suppression of pathogenic microorganisms,
- Stimulation of defense-related metabolites in plants.

These effects are associated with an increase in phenolic and flavonoid content, especially in medicinal plants. However, dose and decomposition time are critical in the use of such materials, and direct and high amount applications may carry the risk of phytotoxicity.

3.4. Biochar and Aromatic Carbon Structures

Biochar is a material with a high aromatic carbon content, which is formed as a result of the pyrolysis of biomass under limited oxygen conditions. Its chemical structure contains concentrated aromatic rings, which gives biochar high stability.

Biochar in organic fertilizer systems:

- Increases the adsorption of nutrient elements,
- Improves soil water holding capacity,
- It provides microhabitat for microbial colonization.

Biochar often functions as an aromatic carbon-based soil amendment rather than a direct fertilizer. When used in combination with compost or organic fertilizers, it creates an indirect fertilizer effect by reducing the washing out of nutrients (Lehmann & Joseph, 2015).

3.5. Formation and Sources of Humic-Like Substances

The aromatic compounds released during composting, green manuring, and biochar applications can break down into humic-like substances over time. These substances have a functional group richness similar to humic acids and can have a biostimulating effect on plant root physiology and nutrient uptake.

Studies in recent years have shown that the biological activity of humic substances is not only the amount; aromatic/aliphatic ratio, phenolic group density and molecular organization (Nardi et al., 2021). This finding shows that the chemical quality of natural fertilizers is at least as important as their nutrient content.

4. Mechanisms of Action of Aromatic Compounds on Soil and Plant

- nutritional intake,
- root formation,
- stress signaling,
- secondary metabolite biosynthesis.

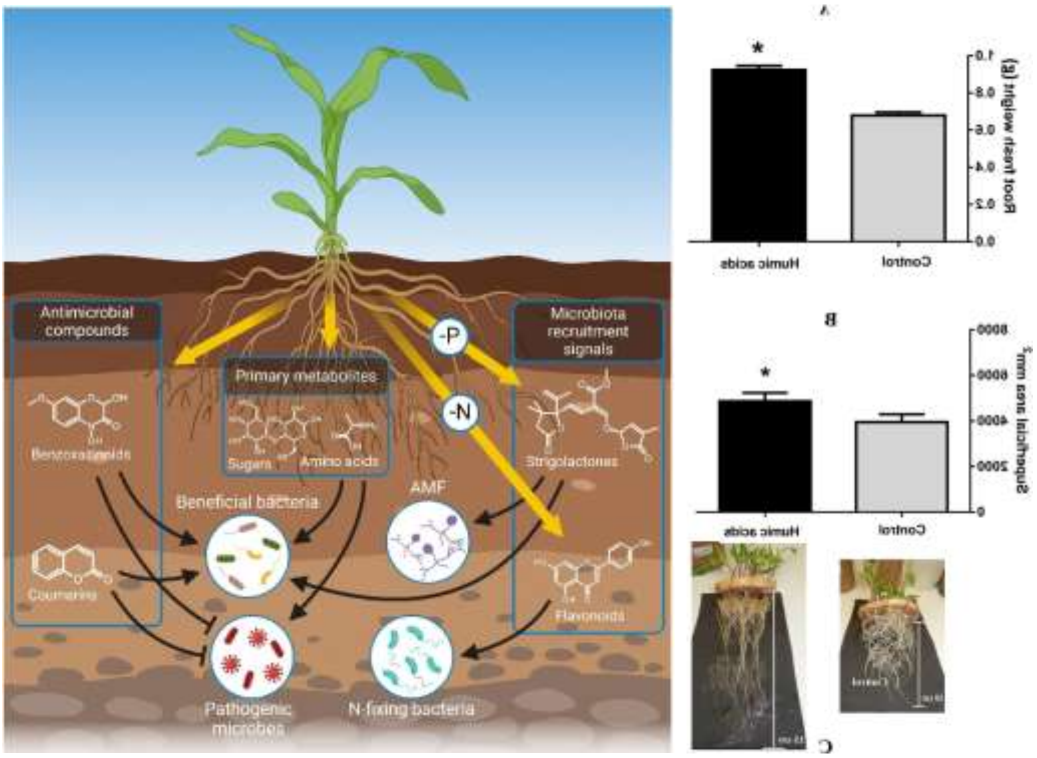

Figure. 4. Root secretions–soil microbiota interaction.

4.1. Effects on Soil Chemistry and Nutrient Dynamics

Aromatic compounds in organic fertilizer systems affect the uptake of nutrients by the plant by regulating soil chemistry rather than providing nutrients directly. Humic substances and compounds containing phenolic structure; It can form complexes with cations (Fe^{2+}, Zn^{2+}, Mn^{2+}, Ca^{2+}) thanks to its carboxyl (–COOH) and phenolic hydroxyl (–OH) groups. This complexation ensures that micronutrients remain soluble in the soil and accessible to the plant (Stevenson, 1994; Marschner, 2012).

The high adsorption capacity of aromatic structures promotes the binding of nutrient elements to soil colloids and their slow release. This reduces sudden nutrient fluctuations, creating a more balanced nutritional profile in plant metabolism. Balanced nutrient supply is critical for the continuity of secondary metabolite synthesis in medicinal plants.

4.2. Interaction with the Rhizosphere Microbiota

Central to the mechanisms of action of aromatic compounds is the rhizosphere microbiota. Phenolic acids and humic compounds can serve as both carbon sources and chemical signals for soil microorganisms. At low concentrations, these compounds promote the activity of beneficial microorganisms; it can alter microbial composition by generating selective pressure at high concentrations (Blum, 1996; Bao et al., 2022).

These changes in the microbiota:

- Food mineralization rate,
- Production of phytohormone-like compounds (e.g. indole derivatives),
- The plant indirectly affects immune responses. Regulation of rhizosphere microbiota, especially in medicinal plants, can increase phenolic and flavonoid biosynthesis via the phenylpropanoid pathway.

4.3. Regulation of Root Formation and Physiology

Humic substances and some aromatic compounds have been shown in many studies to produce morphological changes in the plant root system. Among these changes:

- Increase in the number of lateral roots,
- Increase in root feather density,
- Expansion of root surface area (Canellas & Olivares, 2014; Nardi et al., 2021).

This improvement in root formation allows the plant to take up more nutrients and water from the soil. However, the most important result for pharmacy is that this physiological change increases the metabolic capacity that triggers the production of secondary metabolites in the plant. In other words, the effect of aromatic compounds on the root indirectly shapes the pharmacological quality.

4.4. Stress Signaling and Secondary Metabolite Biosynthesis

Aromatic compounds are often perceived as a mild stress factor in plants . This activates the plant's defense mechanisms, stimulating secondary metabolite synthesis. With the administration of phenolic acids in low doses:

- Phenylalanine ammonium lyase (PAL) activity is increased,
- Accelerated production of phenolics and flavonoids via the phenylpropanoid pathway has been reported (Taiz et al., 2015).

This mechanism explains why organic fertilizers containing aromatic compounds in medicinal plants occasionally increase the amount of active ingredients. However, it should be noted that this effect is extremely sensitive to dose, plant type and environmental conditions.

4.5. Indirect Effects of Biochar and Aromatic Carbon

The intense aromatic carbon structures contained in biochar support the colonization of microorganisms by creating microhabitats in the rhizosphere. These microhabitats are:

- It facilitates the attachment of beneficial microorganisms,
- It provides local concentration of nutrients,
- It strengthens the plant-microbe interaction.

This chain of indirect effects promotes secondary metabolite production by increasing nutrient uptake and stress tolerance in the plant (Lehmann & Joseph, 2015).

4.6. Interpretation of Mechanisms of Action in Terms of Pharmacy

From a pharmaceutical perspective, aromatic compounds' alteration of the chemical profile of herbal products through the mechanisms described above presents both opportunity and risk :

- **Opportunity: Increasing** the amount and diversity of active ingredients,
- **Risk:** Uncontrolled change in the chemical profile.

Therefore, in the application of aromatic compounds used as organic fertilizers:

- The chemical content of the source should be defined,
- Dose and time of administration should be standardized,
- Compliance with GACP principles should be ensured (WHO, 2003; EMA, 2025).

5. Active Ingredient Profile in Medicinal Plants and Effects on Pharmacological Quality

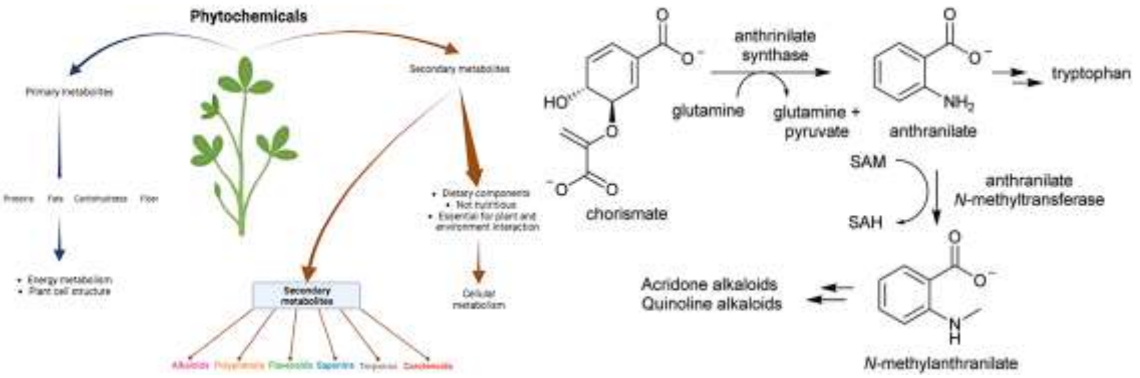

Figure.5. Schematic biosynthetic pathway showing the phytochemical biosynthesis relationship extending from primary metabolites to secondary metabolites in plants and the formation of anthranilate and alkaloid derivatives via the shikimate pathway.

5.1. The Concept of Active Ingredient Profile

The active ingredient profile **in medicinal plants** refers to the type and amount of bioactive compounds present in the plant and the proportional balance of these compounds with each other. This profile; It directly determines the plant's therapeutic effect, standardization potential and pharmaceutical usability. Secondary metabolites such as phenolics, flavonoids, alkaloids, and terpenoids are the main components of the active ingredient profile (Taiz et al., 2015).

Aromatic compounds used as organic fertilizers indirectly shape the active ingredient profile in the plant by regulating metabolic pathways and physiological processes rather than providing molecules directly. Therefore, the effect often **occurs in the form of** qualitative and proportional change rather than "quantitative increase".

5.2. Effects on Phenolic and Flavonoid Compounds

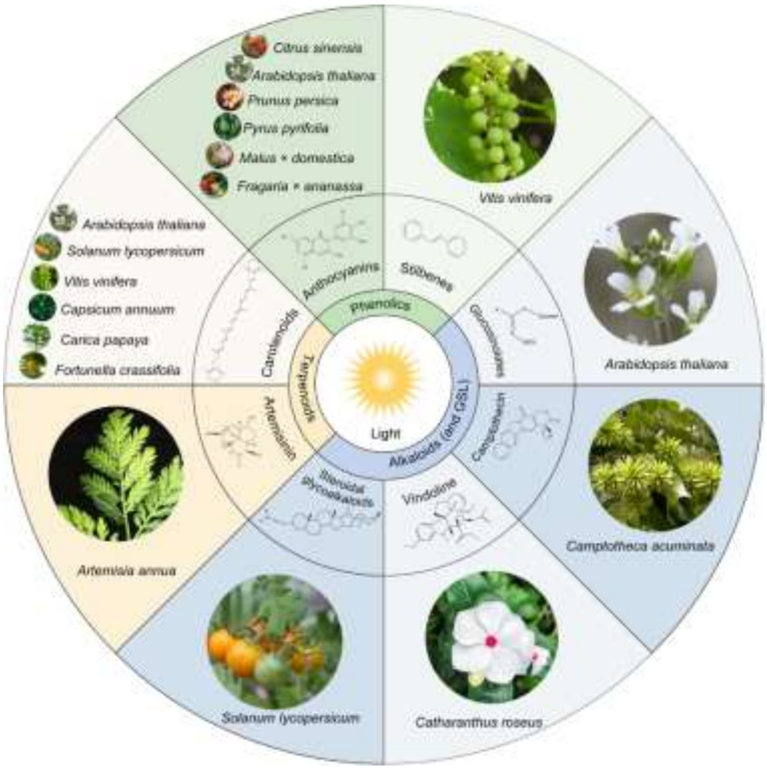

Figure 6. Phytochemical relationship diagram showing the biosynthesis and distribution of major classes of secondary metabolites such as phenolics, terpenoids and alkaloids in different plant species under the influence of light.

Phenolic compounds and flavonoids play central roles in plants' stress responses and defense mechanisms. The biosynthesis of these compounds occurs largely **via the phenylpropanoid** pathway, and the enzyme phenylalanine ammonium lyase (PAL) is a key step in this pathway.

With the application of organic fertilizers containing aromatic compounds:

- Increased PAL activity,
- Increase in total phenolic substance content,
- An expansion of flavonoid diversity has been reported (Blum, 1996; Taiz et al., 2015). This increase strengthens the pharmacological quality in medicinal plants, especially those associated with antioxidant, anti-inflammatory and antimicrobial effects.

However, the literature clearly shows that this effect is **dose-dependent**. Low and moderate aromatic compound inputs produce a stimulating effect, while high concentrations can lead to metabolic suppression and a decrease in phenolic synthesis.

5.3. Alkaloid Biosynthesis and Aromatic Compound Interaction

Alkaloids are nitrogenous organic compounds with strong pharmacological activity and form the basis of the therapeutic action of many medicinal plants. Alkaloid biosynthesis is often closely related to amino acid metabolism and stress response.

Aromatic compounds found in organic fertilizer systems:

- By creating a perception of slight stress in the plant,
- By indirectly affecting nitrogen metabolism,
- It can direct the metabolic flux to alkaloid biosynthesis.

This may result in an increase in the amount of active ingredients in medicinal plants containing some alkaloids. However, this increase is not always linear and varies depending on environmental factors and plant species (Marschner, 2012).

5.4. Terpenoid and Aromatic-Terpene Hybrid Compounds

Terpenoids are an important group of secondary metabolites in plants that play a role in defense, aroma, and biological interactions. The effect of organic fertilizers containing aromatic compounds on terpenoid biosynthesis is generally **through indirect** and **signal-based** mechanisms.

With the application of aromatic plant residues or composts with a high phenolic load:

- Enzyme activity is stimulated in terpenoid synthesis pathways,
- Essential oil composition changes,
- It has been reported that an increase in the proportion of terpenoids associated with pharmacological activity can be seen (Lehmann & Joseph, 2015).

This shows that the quality of essential oils, especially in aromatic and medicinal plants, can be driven by agricultural practices.

5.5. Chemical Profile Variability and Standardization Problem

Variability in the active ingredient profile is one of **the most critical problems** in terms of pharmacy. Uncontrolled or irregular use of aromatic compounds used as organic fertilizers:

- Batch-based chemical differences,
- Fluctuations in active ingredient ratios,
- It can cause pharmaceutical standardization difficulties.

For this reason, aromatic compound-based organic fertilizer applications **should be planned within the framework of GACP principles** and plant raw materials should be verified by analytical methods (such as HPLC, GC-MS, LC-MS) (WHO, 2003; EMA, 2025).

5.6. Overall Impact on Pharmacological Quality and Evaluation

When evaluated in total, it is seen that aromatic compounds used as organic fertilizers in medicinal plants:

- It can increase the amount of active ingredient,
- Enriches chemical diversity,
- However, it is seen that it can lead to quality fluctuations in uncontrolled applications.

Therefore, the integration of these compounds into fertilizer systems should be approached with a focus on quality over quantity. The aim is not maximum active ingredient production; to obtain a consistent, safe and standardizable chemical profile.

6. **Evaluation and Regulatory Dimension in Terms of Pharmacy**

6.1. Quality Expectation in Medicinal Plants as Pharmaceutical Raw Materials

Figure 7. Visual representation of herbal products in different physical forms (powder, granules, extracts and capsules/tablets) obtained from natural raw materials and preparations derived from them.

In terms of pharmaceutical sciences, medicinal plants are not only agricultural products; They are materials that are pharmaceutical raw materials and subject to strict quality requirements in terms of safety and effectiveness. In this context, quality; It covers basic elements such as using the right species and plant part (identity), active ingredient profile (content), contaminants within acceptable limits (purity) and batch-based consistency (standardization).

Since aromatic compounds used as organic fertilizers indirectly affect the chemical profile of plant raw materials, it is imperative that these applications are **controlled and traceable** from the point of view of pharmacy . Otherwise, fluctuations in the active ingredient content and unwanted impurities can adversely affect pharmaceutical quality.

6.2. Use of Organic Fertilizers and Aromatic Compounds within the Framework of GACP

Good Agricultural and Gathering Practices (GACP), developed to ensure quality in the cultivation and collection of medicinal plants, offers a holistic framework that includes organic fertilizer applications. According to the GACP approach:

- The source of agricultural inputs (fertilizer, soil conditioner, biostimulant) should be identified,
- Application dose and time should be recorded,
- Contamination risks (microbial load, heavy metals, residues) should be minimized.

The use of organic fertilizers containing aromatic compounds has a twofold effect in this context . While it can improve pharmacological quality when properly managed, it can lead to chemical profile variability and safety issues in uncontrolled applications. Therefore, GACP principles are particularly critical for aromatic compound-based applications.

6.3. Standardization and Analytical Validation

The availability of herbal raw materials in pharmacy should be supported by analytical verification. Chemical changes that may occur due to the effect of aromatic compounds used as organic fertilizers can be monitored with the following analytical approaches:

- **Chromatographic methods (HPLC, GC-MS, LC-MS):** Determination of marker compounds and fingerprint profiles
- **Spectroscopic methods (UV-Vis, FT-IR):** Monitoring the overall chemical profile
- **Pharmacopoeia tests:** Moisture, ash, extractive, microbial load and heavy metal analysis

These methods are essential tools in ensuring that quality variations associated with agricultural practices remain within pharmaceutical boundaries.

6.4. Contamination Risk and Safety

The use of organic fertilizers and materials containing aromatic compounds poses a risk of contamination for pharmaceuticals . These risks are mainly as follows:

- Microbial contamination (bacteria, mold, yeast)
- Heavy metal accumulation (Pb, Cd, Hg, As)

- Environmental pollutants and unwanted residues

Especially immature composts or plant residues of uncertain origin can increase these risks. Therefore, organic fertilizer applications from a pharmaceutical perspective should be supported by pre-evaluation, monitoring and verification processes.

6.5. Traceability and Farm-to-Pharmacy Approach

The current understanding of pharmaceutical quality is based on the principle of traceability in herbal raw materials . Traceability when it comes to aromatic compounds used as organic fertilizers:

- Documentation of fertilizer source and composition,
- Recording the application conditions (dose, time, method),
- It should be applied in the form of associating it with post-harvest processes. This approach is the most effective way to ensure quality continuity in the chain extending from the "field to the pharmacy".

6.6. General Evaluation in Terms of Pharmacy

From a pharmaceutical perspective, aromatic compounds used as organic fertilizers are:

- **Has the** potential to improve pharmacological quality,
- However, when used uncontrollably, they should be considered as inputs that make standardization difficult.

Therefore, the integration of these compounds into fertilizer systems must be carried out through a measurable approach that is supported by scientific data and aligned with regulatory frameworks. This approach lays the foundation for using medicinal plants as safe, effective, and standardizable pharmaceutical raw materials.

7. Conclusion and Future Outlook

The findings discussed in this section clearly reveal that aromatic compounds used as organic fertilizers should be considered as chemical regulators that direct soil-plant-microorganism interactions, beyond the classical nutrient-based fertilizer understanding. Aromatic structures such as humic substances, phenolic acids, aromatic vegetable residues and biochar; Rather than providing direct N–P–K, it shows an indirect fertilizer effect by increasing the availability of nutrients and regulating plant metabolism.

This indirect effect is of great importance in terms of active ingredient profile and pharmacological quality, especially in medicinal plants. The literature data presented throughout the chapter show that organic fertilizer applications containing aromatic compounds; It reveals that it can stimulate the biosynthesis of secondary metabolites such as phenolics, flavonoids, alkaloids and terpenoids, but this effect varies depending on dose, source, time of administration and plant species.

Figure 8. Visual representation of the holistic effects of soil-plant interaction on nutrient cycling and sustainable agricultural quality with the use of natural and organic inputs in crop production.

7.1. Chemical Quality Bridge Between Agriculture and Pharmacy

One of the main contributions of this study is that it expands the concept of organic fertilizers **from an agriculture-centered yield approach to a pharmacy-centered chemical quality approach**. Aromatic compounds in terms of agricultural sciences; While they are considered as inputs that regulate soil health, microbial activity and plant physiology, the same compounds stand **out as** critical variables affecting the standardization of plant raw materials in terms of pharmaceutical sciences.

For this reason, aromatic compounds used as organic fertilizers function as a **chemical quality bridge** between the two disciplines. When properly managed, these compounds can support both agricultural sustainability and pharmaceutical quality in medicinal plants.

7.2. Limitations and Risks

Although aromatic compound-based organic fertilizer applications offer significant advantages, this approach involves some limitations and risks:

- **Chemical profile variability:** The content of aromatic compounds can vary widely depending on natural sources.
- **Allelopathic effects:** High concentrations of phenolic acids can suppress plant growth.
- **Difficulty in standardization:** It may be difficult to ensure consistency between parties in terms of pharmacy.
- **Risk of contamination: Improperly** treated organic materials can lead to microbial or chemical contamination.

These risks show that the use of aromatic compounds as organic fertilizers should not be carried out randomly, but in a controlled manner based on scientific data.

7.3. Future Outlook

In the future, research into aromatic compounds used as organic fertilizers is expected to focus on the following areas:

1. Metabolomics and systems biology approachesThe effects of aromatic compound applications on the plant metabolite profile will be revealed more holistically through targeted and off-target metabolomics analyses.
2. Aromatic compound-microbiota interactions Elucidating the responses of the rhizosphere microbiota to aromatic compounds will make the fertilizer effect more predictable.
3. Standardized organic fertilizer formulations will be possible to develop controlled and traceable organic fertilizer products with specific aromatic compound profiles.
4. Green pharmacy and sustainable production Organic fertilizer-based approaches will be more strongly integrated with environmentally friendly production models and the concept of "green pharmacy".

Conclusion

In conclusion, aromatic compounds used as organic fertilizers offer an innovative and interdisciplinary field of research that has the potential to enhance the pharmacological quality of medicinal plants. This approach establishes a strong link between agricultural sciences and pharmaceutical sciences; reveals that plant raw materials should be evaluated not only in terms of yield, but also in terms of chemical quality and therapeutic value.

However, in order to realize this potential in a safe and sustainable way; It is imperative that aromatic compound-based organic fertilizer applications are handled within analytically validated and standardized systems that are compatible with GACP principles. Studies to be carried out within this framework will make significant contributions to the future pharmaceutical use of medicinal plants.

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GEÇİCİ KAPAK

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