FROM PLANTS TO HEALTH

CROSS-DISCIPLINARY INSIGHTS

EDITOR

Prof. Dr. Manole COJOCARU

Gheorghe GIURGIU

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TABLE OF CONTENTS

PREFACE

This volume presents a multidisciplinary examination of key scientific and environmental challenges, spanning plant biochemistry, ecological impact assessment, computational modeling, and nutritional science. Each chapter contributes to a broader understanding of how natural systems and technological innovation intersect in shaping sustainable futures.

The first half of the book explores the industrial potential of plant secondary metabolites and the ecological consequences of aero-technogenic emissions in Ukraine’s Sumy region. These studies highlight both the promise of metabolic optimization and the urgency of mitigating anthropogenic stressors on agro-ecosystems.

The latter chapters focus on methodological advances and health-oriented research. Hyperparameter optimization is shown to enhance predictive modeling in socio-environmental systems, while the dual role of certain foods in nutrition and disease prevention underscores the growing relevance of functional foods. Together, these contributions offer integrated insights for science, policy, and public health.

Editoral Team
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CHAPTER 1
PLANT SECONDARY METABOLITES AND THEIR METABOLIC OPTIMIZATION FOR INDUSTRIAL APPLICATIONS

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INTRODUCTION

Natural products (NPs) are chemical compounds derived from living organisms, with origins in microorganisms, plants, or animals. These substances are synthesized through both primary and secondary metabolic pathways. Metabolism refers to the totality of chemical reactions within cells that provide energy for essential biological functions such as growth, development, reproduction, environmental adaptation, and the synthesis of new organic materials. Plant-derived metabolites, which are extensively utilized in agriculture, medicine, and pharmaceuticals, are categorized into two main groups: (i) primary metabolites (PMs) and (ii) secondary metabolites (SMs).

Primary metabolites (PMs) include substances such as carbohydrates, proteins, fats, and alcohols, which are crucial for growth, development, and reproduction (Taiz & Zeiger, 2002; Weinberg & Medicine, 1971; M. J. T. Wink & genetics, 1988). These compounds are produced during the trophophase of plant growth, a phase characterized by rapid production within the organism (Okwu, 1999; Pichersky, Noel, & Dudareva, 2006; Thrane, 2001). PMs are consistently required for various vital processes in the body.

Secondary metabolites (SMs) encompass a vast array of compounds, including over 12,000 alkaloids, 40,000 terpenoids, and 8,000 phenylpropanoids, all of which are primarily produced by plants. The distribution of plant metabolites varies among different taxonomic groups within the plant kingdom. SMs are significant for plant classification, serving as taxonomic markers that distinguish between plant families, genera, and species (Okada et al., 2010; Okwu, 1999). These metabolites play a direct role in plant defense, systemic resistance, and other ecological functions(Balunas & Kinghorn, 2005). Plant secondary metabolites, in particular, serve as vital sources of pharmaceuticals, food additives, and fine chemicals, offering valuable materials for various applications. While natural compounds can be extracted directly from plants, plant cell culture has emerged as a promising alternative for producing metabolites that are difficult to obtain through chemical synthesis or plant extraction (Tiwari, Rana, & Science, 2015). The term "specialized plant metabolites" is increasingly used to describe plant secondary metabolites due to their diversity and multifunctional roles in plant defense, systemic resistance, and growth promotion.

They are classified into three major categories: terpenoids, phenolic compounds, and nitrogen-containing compounds (Balandrin, Klocke, Wurtele, & Bollinger, 1985; Fraenkel, 1959; Samuni-Blank et al., 2012; Savithramma, Rao, & Ankanna, 2011). In addition to their ecological roles, SMs also exhibit protective functions in the human body, such as enhancing the immune system to combat various pathogens. The biosynthesis of SMs is linked to primary metabolic pathways, including the tricarboxylic acid (TCA) cycle, the methylerythritol-4-phosphate (MEP) pathway, and the mevalonic and shikimic acid pathways. The phenylpropanoid pathway, another significant source of plant metabolites, is involved in the biosynthesis of lignin and other crucial compounds such as flavonoids, coumarins, and lignans.

From a metabolic perspective, plant cells produce two types of metabolites: primary metabolites (PMs), which are essential for growth and metabolism (e.g., carbohydrates, lipids, and proteins), and secondary metabolites (SMs), which are the end products of primary metabolites but do not participate directly in metabolic processes (e.g., alkaloids, phenolics, steroids, essential oils, tannins, etc.)(Patwardhan, Vaidya, & Chorghade, 2004). Secondary metabolites serve specialized functions in plant defense and overall plant health (Patwardhan et al., 2004).

Primary metabolites are the primary products of metabolic processes necessary for essential life functions, such as cellular functions, growth, and reproduction. Key examples of PMs include carbohydrates, lipids, proteins, and nucleic acids (Karlovsky, 2008; Rogers, 2010). The production of PMs occurs during the trophophase, when adequate nutrients are available for growth. PMs also play a crucial role in energy production through respiratory and photosynthetic enzymes.

Plants produce a wide variety of organic compounds, many of which do not directly contribute to growth and development. These compounds, known as secondary metabolites, are typically distributed unevenly across different taxonomic groups within the plant kingdom. Recently, the commercial value of secondary metabolites has spurred significant interest in manipulating their production through tissue culture technology (Zhao, Davis, & Verpoorte, 2005).

Plant cell and tissue culture techniques can be routinely established under sterile conditions using explants such as leaves, stems, roots, and meristems.

These cultures can serve both for the multiplication of plant material and for the extraction of secondary metabolites. In fact, in-vitro production of secondary metabolites has been successfully reported in commercial medicinal plants (Zhao et al., 2005).

Secondary metabolites from plants are valuable sources for pharmaceuticals, food additives, flavors, and various industrial products (Zhao et al., 2005). The use of plant cell cultures addresses several challenges associated with producing these metabolites. Organized cultures, especially root cultures, are particularly effective in producing secondary metabolites. These compounds are defined as organic molecules not directly involved in the organism's normal growth, development, or reproduction (Fraenkel, 1959). They are typically produced after the growth phase, may not contribute to growth but could serve survival functions, are produced by specific taxonomic groups of organisms, possess unique chemical structures, and are often present as mixtures of chemically related compounds.

Plant secondary metabolites have garnered significant interest from researchers across plant biology and biotechnology fields. Studies in vitro and in vivo focus on isolating, analyzing, and biochemically characterizing bioactive molecules from various plants to evaluate their biological activity and potential toxicity. Plant secondary metabolites are typically classified into three major chemical classes: terpenoids, phenolic compounds, and nitrogen-containing compounds (Hussein & El-Anssary, 2019).

Unlike primary metabolites, the absence of secondary metabolites does not result in immediate death of an organism. Instead, it leads to long-term consequences, such as reduced survivability, fecundity, aesthetics, or sometimes no significant change at all. Secondary metabolites are often found in a limited set of species within a phylogenetic group and play a crucial role in plant defense mechanisms against herbivory and other interspecies interactions (Samuni-Blank et al., 2012; Stamp, 2003). Humans have long utilized secondary metabolites for various purposes, including medicines, flavorings, and recreational drugs.

Srivastava et al. (2007) pointed out that using differentiated plant cultures, rather than cell suspension cultures, has shifted focus towards transformed (hairy) roots for secondary metabolite production (Srivastava & Srivastava, 2007).

Smetanska (2008) provided a comprehensive multi-stage strategy for obtaining secondary metabolites from plant cell cultures, emphasizing that each step should be tailored to the specifics of the cell cultures or the products being produced (Smetanska, 2008). To establish high-yield, fast-growing cell lines, the selection of parent plants is crucial. Environmental conditions, precursor supply, and elicitor application all influence the expression of synthetic pathways, which can further be modified through treatments like biotransformation and immobilization.

Kossel was the first to distinguish secondary metabolites from primary ones, noting that secondary products are essential for plants' adaptation to their environment. Secondary metabolites have also been recognized for their antibiotic, antifungal, and antiviral properties, which help protect plants from pathogens (Kossel, 1891).

Recent efforts to enhance the production of plant secondary metabolites have focused on several key areas: 1) optimizing plant cell cultures to boost the production of target compounds, by improving chemical processing, bioreactor performance, and the use of elicitors or biotic stressors, regardless of the specific mechanisms involved (Zhong, 2001); 2) investigating signal transduction pathways that drive the effective strategies leading to the biosynthesis of secondary metabolites; 3) exploring transcription factors and their regulatory mechanisms, including the genetic manipulation of regulatory genes to enhance the production of target metabolites (Memelink, Kijne, van der Heijden, & Verpoorte, 2001); 4) cloning secondary metabolite biosynthetic genes and genetically modifying key genes to manipulate metabolic flux toward the desired compounds (Verpoorte & Memelink, 2002); 5) analyzing metabolic flux and profiling intermediates to gain a comprehensive understanding of the entire biosynthetic pathway and the overall regulation of target compound accumulation (Sumner, Mendes, & Dixon, 2003); and 6) profiling gene transcripts involved in secondary metabolism to examine global gene expression under various conditions, which helps in understanding the broader regulation of plant secondary metabolism (Goossens et al., 2003).

Secondary metabolites, a defining characteristic of plants, play a crucial role in protecting plants from a wide range of microorganisms (such as viruses, bacteria, and fungi) and herbivores (including arthropods and vertebrates).

However, similar to the defense systems found in plants and animals, certain specialized pathogens have evolved mechanisms to bypass or overcome these chemical defenses (M. J. T. Wink & genetics, 1988).

1. Overview of Major Classes

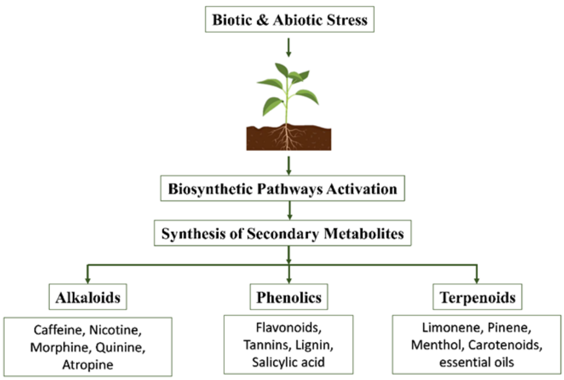

Figure 1. Key Secondary Metabolite Classes in Plants

1.1 Alkaloids

Alkaloids represent one of the most diverse and abundant classes of plant secondary metabolites, found across several economically significant plant families. These compounds include neuroactive substances like caffeine and nicotine, as well as medicinal alkaloids such as emetine, which is used to treat oral intoxications, and vincristine and vinblastine, which serve as antitumor agents. Alkaloids also play a vital role in plant defense, acting as deterrents against pathogens and herbivores due to their toxicity. The ability of plants to detect stressors and adverse environmental conditions quickly, followed by specific signal transduction pathways that trigger alkaloid biosynthesis, is crucial for effective defense mechanisms.

The toxicity of alkaloids is dependent on factors such as dosage, exposure time, individual sensitivity, the action site, and the plant's developmental stage. Depending on the context—whether ecological or pharmacological—these toxic effects can be either detrimental or beneficial.

Various methods are employed to investigate alkaloid metabolism and accumulation, including monitoring gene expression, enzyme activity, and the levels of alkaloid precursors during controlled pathogen and herbivore challenges or their simulated presence via physical or chemical cues. A thorough understanding of alkaloid biosynthesis and their mechanisms of action is vital for enhancing the production of valuable alkaloids, discovering novel bioactive compounds, and sustainably applying them to combat herbivores, pathogens, cancer, or undesirable physiological conditions.

Natural products have been essential to humans for thousands of years, playing key roles in food, medicine, agriculture, and various industrial applications. Alkaloids, a major class of secondary metabolites, are among the most diverse and widely distributed plant compounds, with over 20,000 known varieties found in about 20% of vascular plant species (Yang & Stöckigt, 2010). These nitrogen-containing compounds, characterized by a heterocyclic ring structure with nitrogen, are typically alkaline. Alkaloids are well-known for their significant pharmacological properties, influencing vertebrate organisms in various ways.

Alkaloids can be classified into numerous categories based on their biosynthetic origin, such as indole alkaloids derived from tryptophan. Other examples include tropane, pyrrolidine, and quinolizidine alkaloids, among many others (Yang & Stöckigt, 2010). These compounds contribute to plants' defense mechanisms, helping them withstand biotic and abiotic stressors, and also play a role in facilitating plant-pollinator interactions. Alkaloids can deter herbivores through toxicity or bitterness, while certain compounds can attract pollinators, enhancing reproductive success. Additionally, alkaloids and other secondary metabolites can stimulate or regulate pollinator visits, improving plant survival rates. Their diverse biological activities extend to humans, offering therapeutic benefits such as antioxidant properties, anticancer agents, analgesics, and stimulants (Yang & Stöckigt, 2010).

The primary ecological function of alkaloids is defense against herbivores. Many alkaloids disrupt protein function or affect the central nervous system of herbivores upon ingestion, making them effective deterrents (J. B. Harborne, 1993). To prevent self-intoxication, plants often store these compounds in vacuoles or apoplastic spaces, reducing their metabolic activity and minimizing harm to the plant itself (Mithöfer & Boland, 2012).

Alkaloids are among the most significant and historically impactful groups of plant-derived compounds, particularly in the field of medicine. The isolation of morphine by Friedrich Wilhelm Sertürner in 1806 marked a milestone in the study of plant secondary metabolites and is considered the formal beginning of plant metabolism research (Hartmann, 2007). While alkaloids primarily serve as toxic defense mechanisms in plants, protecting them from herbivores and pathogens, these same toxic properties are often leveraged in drug development. For example, alkaloids with specific toxicities are being explored for their potential in targeting cancer cells and controlling harmful microorganisms or pests (Lee et al., 2014; Yang & Stöckigt, 2010).

Historically, plant alkaloids have been used in a wide range of ways, from medicinal and therapeutic to recreational and religious purposes. Several alkaloids affect the human central nervous system (CNS), which is why they have been used for sensory alteration since ancient times. For instance, the latex of the opium poppy (Papaver somniferum) was used as early as 1400–1200 B.C. in the Eastern Mediterranean. Similarly, the roots of Rauvolfia serpentina have been used in India for millennia, dating back to approximately 1000 B.C. In ancient Greece, the philosopher Socrates was executed by ingesting an extract of hemlock (Conium maculatum), and Cleopatra is said to have used henbane (Hyoscyamus) for its atropine content to dilate her pupils for cosmetic purposes. During the Middle Ages, certain tropane alkaloids derived from plants in the Solanaceae family were believed to have magical properties and were used by witches in various rituals (Croteau, Kutchan, Lewis, & plants, 2000).

In modern times, alkaloids continue to be both beneficial and hazardous. Caffeine, found in coffee (Coffea arabica), tea (Camellia sinensis), and cocoa (Theobroma cacao), is a stimulant widely consumed for improving mental alertness and physical performance.

Nicotine, another CNS stimulant, is commonly consumed through tobacco products such as cigarettes and cigars (Nicotiana tabacum). Morphine remains one of the most effective analgesics, while codeine, derived from the same plant, is commonly used as a sedative and cough suppressant. However, alkaloids like cocaine (Erythroxylum sp.) pose significant societal challenges due to their addictive properties and the illegal trade associated with them (Koleva et al., 2012; Senchina, Hallam, Kohut, Nguyen, & Perera, 2014).

Strychnine, extracted from Strychnos nux-vomica, is a potent neurotoxin that is used as a rat poison and in homeopathic remedies (Croteau et al., 2000).

In agriculture, alkaloids can serve as natural deterrents to herbivores, reducing the need for pesticides. For example, Lupinus species, which contain quinolizidine alkaloids, are less palatable to herbivores, leading to reduced pesticide applications in crops grown with these varieties (del Pilar Vilariño, Ravetta, & Botany, 2008). In contrast, crops like tomatoes that lack such defensive compounds require higher pesticide use. Interestingly, crops that have not undergone extensive artificial selection, especially those focused on edible parts for human consumption, may still retain useful alkaloid-based defense mechanisms, allowing them to thrive with fewer agricultural inputs. Some alkaloids also exhibit allelopathic effects, inhibiting the growth of other plants. For example, alkaloids like berberine, sanguinarine, and gramine have been shown to inhibit seedling growth in Lactuca sativa and Lepidium sativum (M. Wink & Twardowski, 1992), though their potential for use in weed control remains to be fully explored.

Alkaloids also play an important ecological role beyond plant defense. Some animals, such as poison frogs (Dendrobatidae) in South and Central America, acquire toxic alkaloids indirectly by consuming alkaloid-containing arthropods. These frogs store alkaloids such as chimonanthine, calycanthine, and nicotine in their skin, which serves as protection against predators (Saporito, Donnelly, Spande, & Garraffo, 2012). Similarly, it was once believed that Bufonidae frogs produced their own alkaloids, but recent studies have shown that they too acquire these compounds through their diet (Hantak et al., 2013). Certain species of Phyllobates frogs can secrete batrachotoxins, some of the most potent neurotoxins known (Zhang et al., 2014).

Additionally, the larvae of Utetheisa ornatrix (bella moth), which feed on Crotalaria species, store pyrrolizidine alkaloids that protect them from predators and are passed on to females as nuptial gifts, which are transferred to the eggs, further protecting the next generation from predation (Eisner, 2005).

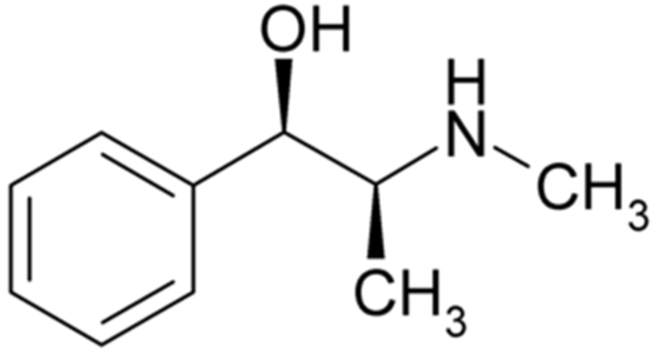

Figure 2. Chemical structure of Alkaloids (Adapted from Wikipedia)

1.1 Phenolics

Numerous secondary metabolites are produced by plants and are categorized into various classes based on their structural characteristics and biosynthesis pathways. The most prevalent secondary metabolites in the plant world are phenolic compounds; it is estimated that 2% of all carbon photosynthesized by plants, or roughly 1 x 10^{o} t annually, is transformed into flavonoids or closely similar molecules (Robards & Antolovich, 1997). The terms 'phenol' and 'polyphenol can be defined chemically as substances that possess an aromatic ring bearing one (phenol) or more (polyphenol) hydroxyl substituents, but in the context of plant phenolics, such a definition is not satisfactory since it would include compounds such as the phenolic carotenoid 3-hydroxy isorenieratene or the phenolic female sex hormone estrone, which are principally terpenoid in origin (Harborne, 1989a).

Food composition databases for macro- and micronutrients provide essential information for research on the health effects of nutrients, nutritional surveillance, clinical dietetic practice and food formulation and processing. However, analogous compositional information on potentially bioactive phytochemicals, including phenolic acids, in foods is generally lacking.

Plants encounter numerous pests and pathogens in the natural environment. An appropriate response to attack by such organisms can lead to tolerance or resistance mechanisms that enable the plant to survive. Resistance mechanisms refer to traits that inhibit or limit attack, while tolerance strategies do not limit attack but reduce or offset the consequences to the plant's fitness by adjusting its physiology to buffer the effects of herbivory or diseases. Resistance strategies include physical and/or chemical barriers, mechanisms that rapidly clear infection or herbivory (hypersensitive response), and processes that limit the spread of damage within the host (such as localized cell death). Tolerance often involves some degree of compensation for disease damage. Plants can tolerate infection or herbivory by increasing the chlorophyll concentration in leaves, increasing the size of new leaves or the number of new branches, advancing the timing of bud break, delaying the senescence of infected tissues, and increasing the uptake of nutrients (Roy & Kirchner, 2000). Most plants produce a broad range of secondary metabolites that are toxic to pathogens and herbivores, either as part of their normal program of growth and development or in response to biotic stress. Preformed antibiotic compounds that occur constitutively in healthy plants are likely to represent inbuilt chemical barriers to herbivorous and fungal enemies and may protect plants against attack by a wide range of potential pests and pathogens. In contrast, induced defense compounds are synthesized in response to biotic stress as part of the plant's defense response and are restricted to the damaged tissue. Both tolerance and resistance traits require the reallocation of host resources; therefore, defensive chemicals are considered to be costly for plants, reducing the fitness of the host in the absence of disease because resistance (R) genes might impose metabolic costs on plants (e.g., lower growth rates than their sensitive counterparts).

There is considerable current interest in plant phenolics and their potential to beneficially affect human health. This interest spans from academics and health professionals to food producers and processors and reflects the interest in dietary components that offer benefits beyond nutrition (i.e., nutrients at levels sufficient to prevent disease due to deficiency) and may prevent degenerative diseases and prolong life.

In fact, there is an inverse association between the consumption of plant foods and risk for a number of age-related diseases (Van Dam, Willett, Rimm, Stampfer, & Hu, 2002).

Plant phenolics exhibit a range of biological activities in vitro, which supports their contribution to the beneficial effects of fruit and vegetable-rich diets. Indeed, there is reasonable evidence from epidemiological studies to support the notion that diets rich in phenolics (derived from fruits and vegetables) are associated with lower risks of cancer, osteoporosis, cardiovascular diseases, cataracts, and diseases associated with brain and immune dysfunction. Furthermore, phenolic compounds, which constitute the active substances found in commonly used medicinal plant extracts, modulate the activity of a wide range of enzymes and cell receptors (Middleton et al., 2000; Pietta, 2000; Manach et al., 2004; Arts & Hollman, 2005; Scalbert et al., 2005). One possible reason for this protection against diseases may be the powerful antioxidant and free radical scavenging properties of various classes of phenolic compounds, although it is worth noting that the physiological relevance of direct antioxidant action as a mechanism to explain the impact of phenolics on disease risk has been questioned (Cook & Samman, 1996; Halliwell, 2006; Hertog, Feskens, Kromhout, Hollman, & Katan, 1993; Prior & Cao, 2000; Rice-Evans, Miller, & Paganga, 1997). However, much of the evidence concerning the mechanism of disease prevention by phenols and polyphenols is derived from in-vitro experiments, which are performed with doses higher than those to which humans are exposed through the diet. In this connection, only partial information is available on the quantities of dietary phenolics that are consumed daily throughout the world (Manach, Scalbert, Morand, Rémésy, & Jiménez, 2004). In addition, the active compounds may not be the native phenolics found in food, as most polyphenols are present in food in the form of esters, glycosides, or polymers, and these compounds must be hydrolyzed in the human body before they can be absorbed. During the course of absorption, phenolic aglycones are conjugated in the small intestine and, later, in the liver, and this process includes glucuronidation, methylation, and sulfation.

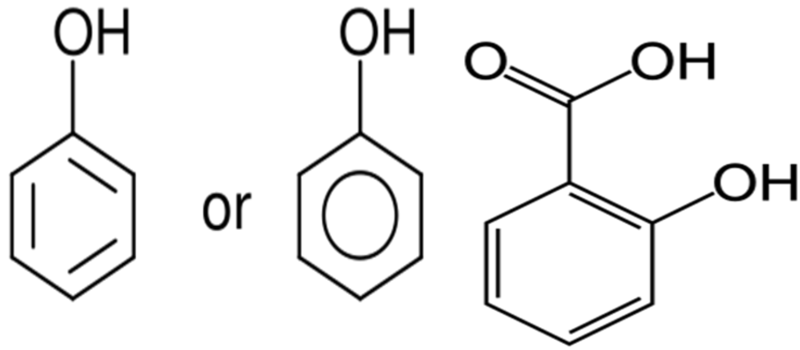

Figure 3. Chemical structure of Phenolics (Adapted from Wikipedia)

1.3 Terpenoids

Among plant secondary metabolites terpenoids are a structurally most diverse group; they function as phytoalexins in plant direct defense, or as signals in indirect defense responses which involve herbivores and their natural enemies. In recent years, more and more attention has been paid to the investigation of the ecological role of plant terpenoids. The biosynthesis pathways of monoterpenes, sesquiterpenes, and diterpenes include the synthesis of C5 precursor isopentenyl diphosphate (IPP) and its allylic isomer dimethylallyl diphosphate (DMAPP), the synthesis of the immediate diphosphate precursors, and the formation of the diverse terpenoids. Terpene synthases (TPSs) play a key role in volatile terpene synthesis (Cheng et al., 2007).

Terpenoids, which constitute the most abundant and structurally diverse group of plant secondary metabolites, play an important role in plant-insect, plant-pathogen, and plant-plant interactions (N. Dudareva, E. Pichersky, & J. Gershenzon, 2004a). Terpenoids are commonly present in higher plants and more than 23 000 individual structures have been identified. Terpenoids are normally produced in vegetative tissues, flowers, and, occasionally, roots (Dudareva et al., 2004a).

Terpenes (pinene, myrcene, limonene, terpinene, p-cymene) are characterized as compounds with simple hydrocarbons structures while terpenoids (oxygen-containing hydrocarbons) are defined as modified class of terpenes with different functional groups and oxidized methyl groups moved or removed at various positions (Perveen, Al-Taweel, & terpenoids, 2018).

Plants have direct and indirect defense responses when they are attacked by herbivores or infected by fungal and bacterial pathogens. Direct defenses include physical structures, such as trichomes and thorns, and the accumulation of chemical or biochemical compounds that have antibiotic activities or toxicities. Phytoalexins are low-molecular-weight compounds that are produced as part of the plant defense system. Indirect defenses indicate the phenomenon that plants have characteristics to defend against herbivores indirectly by enhancing the effectiveness of the natural enemies of the herbivores. These constitutive or inducible characteristics also include physical structures and chemical features. One of the most amazing examples of the plant's indirect defense is the release of a blend of specific volatiles, which attract the carnivores of herbivores, after the herbivore attacks. In recent years, intensive attention has been paid to this indirect defense reaction, particularly of corn, lima bean, poplar, and cotton that are well studied with genetic, biochemical, physiological, and ecological approaches (Rodriguez-Saona, Crafts-Brandner, & Cañas, 2003). Research in maize revealed that caryophyllene emitted from roots was a herbivore-induced underground signal that strongly attracts entomopathogenic nematodes. It has been previously demonstrated that shoots of Lotus japonicus infested with spider mites (Tetranychus urticae) release a blend of volatiles, which are attractive to predator mites (Phytoseiulus persimilis).

In recent decades, numerous studies have reported that terpenes and terpenoids are essential in supporting human health. Essential oils (EOs) have been one of the most utilized natural products (Carpena, Nuñez-Estevez, Soria-Lopez, Garcia-Oliveira, & Prieto, 2021). Essential oils are highly concentrated hydrophobic liquids derived from a variety of plants and defined based on their chemical and physical properties.

The pharmacological effect of EOs have been extensively examined: ranging from antimicrobial (Burt, 2004; Falleh, Jemaa, Saada, & Ksouri, 2020), antihelminthic (Inouye, Yamaguchi, & Takizawa, 2001), antiviral (Da Silva, Figueiredo, Byler, & Setzer, 2020), antiulcer (Đorđević et al., 2007), antioxidant (Falleh et al., 2020) and antinociceptive properties (Abdollahi, Karimpour, & Monsef-Esfehani, 2003). Essential oils have long been used as flavorings in the food industry (Pandey, Kumar, Singh, Tripathi, & Bajpai, 2017). Of thousan ds different EOs known at present, around 300 are commercially marketed in the flavor and fragrances products (Hyldgaard, Mygind, & Meyer, 2012). In addition to their aromatic qualities, the antimicrobial properties of EOs against a wide range of microorganisms have also provided convincing evidence that EOs are suitable candidates to be used as natural food preservatives (Falleh et al., 2020). Among all chemical components of EOs, terpenes and terpenoids have been comprehensively studied and reported to play key roles in human health (Perveen et al., 2018).

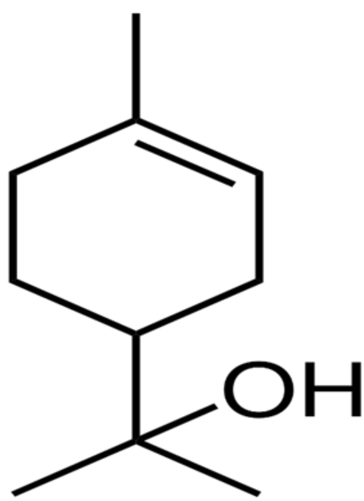

Figure 4. Chemical structure of Terpenoids (Adapted from Wikipedia)

Table 1. Plant Secondary Metabolites: Sources, Applications, and Examples

Category	Sources	Applications	Examples	References
Alkaloids	-various plant families such as Solanaceae, Papaveraceae and Fabaceae	-medicinal purpose (anticancer, analgesic, stimulant) -pest control -neurological treatments	Morphine (*Papaver somniferum*), Caffeine (*Coffea arabica*), Nicotine (*Nicotiana tabacum*)	(J. J. N. P. R. Harborne, 1993; Matsuura & Fett-Neto, 2015)
	-toxic plants as a defense mechanism against herbivores	-agriculture -pharmaceuticals	Vinblastine (*Catharanthus roseus*), Strychnine (*Strychnos nux-vomica*)	(M. Wink & Twardowski, 1992)
	-response to environmental stress -response toherbivore attacks	-anti-inflammatory, analgesic and antimicrobial activities	Emetine (*Cephaelis ipecacuanha*), Reserpine (*Rauvolfia serpentina*)	(Saporito et al., 2012); (Croteau et al., 2000)
Phenolics	- fruits -vegetables -cereals -tea -red wine	-antioxidants, -anti-inflammatory, -antimicrobial agents -beneficial for cardiovascular health	Quercetin (onions, apples), Resveratrol (grapes, red wine), Tannins (tea, grapes)	(Harborne, 1989b; Robards & Antolovich, 1997)
	-produced in plants as a response to UV radiation, pathogens, and herbivores	-food preservation -cosmetics -disease prevention	Lignins (woody plants), Flavonoids (*Citrus spp.*), Anthocyanins (berries)	(Halvorsen et al., 2002b); (Dimitrios & technology, 2006)
	-allelopathic agents to inhibit the growth of competing plants	-sustainable agriculture -weed control	Juglone (walnut trees), Coumarins (Tonka beans)	(John & Sarada, 2012)
Terpenoids	-essential oils of aromatic plants such as mint, lavender and citrus	-pharmaceuticals - cosmetics -perfumery -agriculture (insect deterrents)	Limonene (citrus fruits), Myrcene (mangoes), Pinene (pine trees)	(N. Dudareva, E. Pichersky, & J. J. P. p. Gershenzon, 2004b)
	-attract pollinators and seed-dispersing animals	-fragrance -ecological balance	Floral Volatiles (*Orchidaceae*), Carotenoids (carrots, tomatoes)	(Leonhardt, Baumann, Wallace, Brooks, & Schmitt, 2014)
	-defensive compounds against herbivores and pathogens	-agriculture (biopesticides) -medicine (antimicrobial properties)	Artemisinin (*Artemisia annua*), Taxol (*Taxus brevifolia*)	(Divekar, Narayana, Divekar, Kumar, Gadratagi, Ray, Singh, Rani, Singh, & Singh, 2022)

2. Roles of Secondary Metabolites in Plants

2.1 Biological Function

2.1.1 Anti-microbial

Plant secondary metabolites (SMs) with antimicrobial properties against various pathogens include saponins, flavonoids, thiosulfinates, glucosinolates, phenolic compounds, alkaloids, and organic acids. The antimicrobial effectiveness of these compounds is influenced by their chemical structure, primary constituents, and the dosage used.

Among these, certain terpenoids (such as aliphatic alcohols, aldehydes, ketones, and acids) and phenolic compounds (including isoflavonoids) are particularly important in exhibiting strong antimicrobial effects (Hussein & El-Anssary, 2019). The antibacterial activity of over 40 plant extracts has been linked to the presence of phenolic compounds. Additionally, vegetables like red cabbage, which contain anthocyanins, a type of phenolic compound, have shown promising antimicrobial properties (Hafidh et al., 2011; Shan, Cai, Brooks, & Corke, 2007).

2.1.2 Anti-oxidant

Antioxidants are compounds that inhibit the oxidation process, a chemical reaction that can generate free radicals and chain reactions, potentially causing cellular damage. These substances are important for enhancing the quality of processed foods and preventing spoilage (Poljsak, Kovač, & Milisav, 2021). Antioxidants can be derived from both natural and synthetic sources. Certain fruits and vegetables are particularly rich in antioxidants within their tissues (Elshafie, Camele, & Mohamed, 2023). Plant secondary metabolites (SMs) with potential antioxidant activity present natural alternatives to synthetic chemicals for improving food quality and extending shelf life (Dimitrios & technology, 2006; Jiang & Xiong, 2016). Various plant families, such as Asteraceae, Rosaceae, and Punicaceae, produce bioactive SMs, including flavonoids, lignans, vitamins, carotenoids, and terpenoids, all of which exhibit strong antioxidant properties (Halvorsen et al., 2002a).

The primary natural antioxidants found in plant materials are polyphenols (such as phenolic acids, flavonoids, anthocyanins, lignans, and catechins), carotenoids (including xanthophylls, lycopene, and carotenes), and vitamins (such as vitamins E and C).

2.1.3 Antibiotic

Several plant secondary metabolites (SMs) possess antibiotic properties, targeting essential cellular functions like cell wall synthesis, DNA/RNA replication, and protein synthesis in harmful microorganisms. From 1935 to 1968, 12 antibiotics were introduced into medical practice (Robbel & Marahiel, 2010). However, antibiotic development slowed significantly between 1969 and 2000. The situation improved again from 2003 to 2015, with 20 new antibiotics approved, 16 of which were derived from natural compounds or their derivatives (Kumar & Pandey, 2013).

Notable recent antibiotics from natural sources include fidaxomicin (2010) and daptomycin (2003), which are derived from Actinomycetes, and retapamulin (2007), a pleuromutilin extracted from fungi such as Pleurotus mutilus, Pleurotus passeckerianus, and Clitopilus scyphoides (Robbel & Marahiel, 2010). In a study by Newman and Cragg (Kumar & Pandey, 2013), it was reported that several plant SMs, such as plazomicin and sisomicin, both aminoglycoside derivatives, were approved in the USA. They also mentioned that in 2018, modifications to aminoglycosides led to the development of tetracycline-based antibiotics, including omadacycline, eravacycline, sarecycline, and lefamulin (Kumar & Pandey, 2013).

2.1.4 Anti-viral

There is currently no highly effective therapy for viral infections because viruses rely on the host cell’s biological mechanisms for replication, making any treatment potentially harmful to the host cells and often associated with serious side effects (El Sayed, 2000). Natural compounds are being explored as valuable sources for the discovery and development of new antiviral drugs, mainly due to their availability and relatively low side effects.

Although there are few plant-derived antiviral drugs available for treating viral diseases, research into new plant sources with antiviral potential is ongoing (Clark, 1996). A report on medicinal chemistry from 1983 to 1994 indicated that only seven out of ten FDA-approved natural drugs were derived from plant sources, compared to synthetic agents. Many natural and synthetic compounds have shown antiviral activity in vitro, but their effectiveness in vivo remains limited (El Sayed, 2000). Much of the research on antiviral compounds focuses on inhibiting various enzymes involved in the viral life cycle.

2.1.5 Anti-inflammatory

Inflammation is a complex biological defense mechanism that occurs in response to microbial infections, tissue damage, or irritants. It involves immune cells, blood vessels, and various molecular mediators (Kumar & Pandey, 2013).

Several studies have highlighted the anti-inflammatory effects of natural herbs, such as Curcuma longa, Zingiber officinale, Rosmarinus officinalis, and Borago officinalis, which show promising potential for clinical applications (Ghasemian, Owlia, Owlia, & Sciences, 2016). Recently developed natural products as anti-inflammatory drugs offer a valuable resource, including detailed explanations and molecular docking strategies for naturally occurring compounds with anti-inflammatory activity (Beg, Swain, Hasan, Barkat, & Hussain, 2011; Sammar, Abu-Farich, Rayan, Falah, & Rayan, 2019). Plant secondary metabolites (SMs), including polyphenols, terpenes, fatty acids, and other bioactive components, have also shown significant anti-inflammatory effects. Specifically, Plant-derived compounds such as moupinamide (from Zanthoxylum beecheyanum), capsaicin (from chili pepper), and hypaphorine (from Erythrina velutina) have potential as new and promising anti-inflammatory drugs (Aswad et al., 2018).

2.2 Ecological Function

2.2.1 Defence Against Herbivores (Insects, Vertebrates)

Plant secondary metabolites play a crucial role in ecological defense, acting as a chemical arsenal against a diverse range of herbivores, from insects to vertebrates (Divekar, Narayana, Divekar, Kumar, Gadratagi, Ray, Singh, Rani, Singh, Singh, et al., 2022).

These compounds, not essential for basic plant metabolism, have evolved to deter herbivory through various mechanisms. For instance, terpenoids, such as those found in conifers, can act as potent insect repellents, while alkaloids like nicotine in tobacco plants are toxic to many herbivores, disrupting their nervous systems. Phenolic compounds, such as tannins, reduce the digestibility of plant tissues, making them less palatable to vertebrates (Pratyusha, 2022). These chemical defenses can be constitutive, meaning they are always present, or induced, produced in response to herbivore attack. This dynamic defense system highlights the intricate evolutionary arms race between plants and their herbivores, where the production of diverse secondary metabolites enhances plant survival and fitness. These metabolites therefore are a very important factor in the ecological function of plants (Alami, Guo, Mei, Yang, & Wang, 2024).

2.2.2 Defence Against Fungi, Bacteria and Viruses

Plant secondary metabolites serve as a critical component of a plant's defense system against a wide array of pathogens, including fungi, bacteria, and viruses (Pang et al., 2021). These compounds, often with antimicrobial properties, act as chemical barriers, inhibiting pathogen growth and spread(Jeandet, Vasserot, Chastang, & Courot, 2013). For example, phytoalexins, a class of secondary metabolites, are produced in response to pathogen attack, acting as potent antifungal and antibacterial agents (Jeandet et al., 2013). Phenolic compounds, such as flavonoids and tannins, can disrupt microbial cell membranes and interfere with viral replication (Hierholtzer, Chatellard, Kierans, Akunna, & Collier, 2013). This chemical defense mechanism is essential for plant survival, highlighting the vital ecological role of secondary metabolites in protecting plants from microbial threats. These compounds are a key part of the plant's immune system (Pang et al., 2021).

2.2.3 Defence Against Other Plants Competing for Light, Water And Nutrients

Plant secondary metabolites play a significant role in interspecific competition, acting as allelochemicals that inhibit the growth and establishment of neighboring plants, thus securing resources like light, water, and nutrients (McCoy, Widhalm, & McNickle, 2022).

This form of chemical warfare, known as allelopathy, allows plants to create a competitive advantage in their environment (McCoy et al., 2022). For example, juglone, a naphthoquinone produced by walnut trees, inhibits the germination and growth of many plant species in its vicinity. Similarly, certain phenolic acids and flavonoids released by plants can suppress the root development and nutrient uptake of competing vegetation. These allelochemicals can be released into the environment through root exudation, leaf litter decomposition, or volatilization, effectively creating a zone of inhibition around the producing plant (Kong, Li, Li, Xia, & Wang, 2024). This ecological function highlights the importance of secondary metabolites in shaping plant community structure and dynamics, enabling plants to dominate their surroundings through chemical interference (Akbar et al., 2024).

2.2.4 Signal Compounds to Attract Pollinating and Seed-Dispersing Animals

Plant secondary metabolites are not solely defensive; they also play a vital role in attracting beneficial animals for pollination and seed dispersal, thus ensuring reproductive success. These compounds act as signal molecules, creating olfactory and visual cues that guide animals to flowers and fruits. For instance, volatile organic compounds (VOCs), such as terpenes and esters, produce the characteristic scents of flowers, attracting pollinators like bees and butterflies. Similarly, colorful pigments, such as anthocyanins and carotenoids, give fruits their vibrant hues, signaling ripeness and nutritional value to seed-dispersing animals like birds and mammals. These secondary metabolites can be highly specific, attracting particular pollinators or seed dispersers based on their preferences. For example, some orchids produce scents that mimic the pheromones of specific insects, attracting them for pollination.

Thus, secondary metabolites facilitate crucial ecological interactions, promoting plant reproduction and contributing to the intricate web of life (Wang et al., 2023).

2.2.5 Signals for Communication Between Plants and Symbiotic Microorganisms (N-Fixing Rhizobia or Mycorrhizal Fungi)

Plant secondary metabolites are essential for establishing and maintaining symbiotic relationships with beneficial microorganisms, such as nitrogen-fixing Rhizobia and mycorrhizal fungi. These compounds act as crucial signaling molecules, facilitating communication and mutualistic interactions. For example, flavonoids released by legume roots serve as chemoattractants, guiding Rhizobia bacteria towards the root surface and triggering the expression of nodulation genes. Similarly, strigolactones, a class of plant hormones, stimulate the branching and growth of mycorrhizal hyphae, promoting colonization of the root system. These signaling molecules ensure a specific and efficient interaction, enabling plants to acquire essential nutrients like nitrogen and phosphorus from the soil. The intricate chemical dialogue between plants and symbiotic microorganisms, mediated by secondary metabolites, underscores the vital ecological role these compounds play in nutrient cycling and plant health (Cianciullo, Maresca, Sorbo, & Basile, 2021).

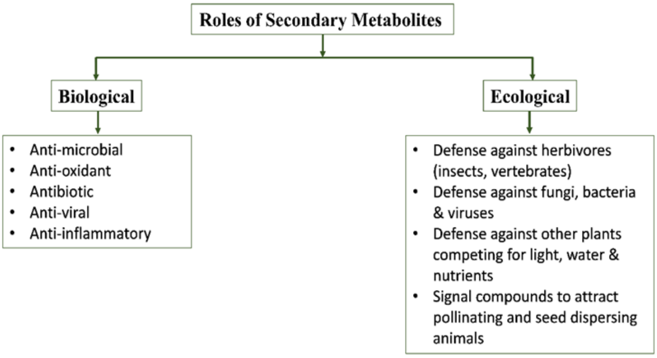

Figure 5. Biological and Ecological Roles of Secondary Metabolites in Plants

CONCLUSION

Plant secondary metabolites (PSMs) are a diverse group of organic compounds produced by plants that play essential roles in defense, ecological interactions and adaptation to environmental stress. These metabolites, including alkaloids, terpenoids, flavonoids, and phenolics, exhibit a wide range of biological activities, such as antioxidant, anti-inflammatory, antimicrobial, anticancer, and neuroprotective effects, making them highly valuable for therapeutic applications. PSMs hold promise for addressing global health challenges, including antibiotic resistance, cancer, and neurodegenerative diseases. However, the complex biosynthetic pathways and regulatory mechanisms involved in PSM production present significant challenges in harnessing their full therapeutic potential. Recent advancements in metabolic engineering and synthetic biology have provided innovative strategies to overcome these limitations, enabling the manipulation of plant metabolic pathways to enhance PSM production and create novel bioactive compounds with improved properties. By integrating knowledge from plant biochemistry, genetics, and synthetic biology, researchers are optimizing the sustainable production of valuable PSMs for use in the pharmaceutical, agricultural, and food industries. This chapter explores the therapeutic potential of PSMs, focusing on their mechanisms of action, clinical applications, and the challenges involved in their development as drug candidates.

It also highlights the role of metabolic engineering in improving PSM yields and creating novel compounds, offering new opportunities to address pressing global health issues and advance the use of plant-derived therapeutics in various industries.

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CHAPTER 2
IMPACT OF AERO-TECHNOGENIC EMISSIONS ON NATURAL AND AGRO-ECOSYSTEMS IN SUMY REGION, UKRAINE

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INTRODUCTION

Aero-technogenic emissions from industrial enterprises are among the key factors of anthropogenic environmental pollution, exerting a significant impact on both natural and agro-ecosystems. Their influence is manifested in the transformation of the physicochemical properties of soils, alterations in the structure of plant communities, reduced productivity of agricultural crops, and overall deterioration of biotic quality (Vakal & Didukh, 1991, 1992; Bashtannik et al., 2014; Savenets et al., 2019; Hodinchuk et al., 2021; Solokha et al., 2024; Ministry of Environmental Protection of Ukraine, 2021).

Studies conducted worldwide have demonstrated that elevated concentrations of sulfur dioxide, hydrogen fluoride, and other pollutants in the air and soil disrupt the functioning of biogeocenoses, damage the foliage of woody and herbaceous plants, and decrease soil fertility (Kharytonov et al., 2017; Fedoniuk et al., 2019; Leal Filho et al., 2024). The negative effects of airborne pollutants include acidification of soils, reduced microbial activity, and impaired nutrient cycling, which collectively contribute to diminished ecosystem stability and agricultural productivity (Vakal & Poroshina, 2010; Kasyanenko & Matsak, 2022; Solokha et al., 2024; Leal Filho et al., 2024).

In Sumy region, where chemical enterprises and highly productive agricultural lands are concentrated within relatively small areas, the issue of the complex impact of industrial emissions on ecosystems is particularly relevant. Considering the additional negative effects of ongoing military activities, which further deteriorate soil conditions and vegetation cover, such research acquires considerable practical importance. The present study gives balanced attention to the assessment of soils, natural forest phytocoenoses, and agrocenoses, particularly the yield of winter wheat, within the zone affected by industrial aero-technogenic emissions (Vakal & Didukh, 1991, 1992; Bashtannik et al., 2014; Savenets et al., 2019; Hodinchuk et al., 2021; Ministry of Environmental Protection of Ukraine, 2021; Kabylda et al., 2024; Solokha et al., 2024).

The aim of this study is to evaluate the transformation of soil physical properties, vegetation cover structure, and winter wheat yield in the zone of influence of aero-technogenic emissions in Sumy region in 2023, and to compare the obtained results with data from previous observations beginning in 1989.

1. Materials & Methods

The data presented in this study were obtained during field investigations conducted within the area influenced by industrial emissions from PJSC "Sumykhimprom." Long-term monitoring in this region has been ongoing since 1989. The results obtained in 2023 were compared with historical data collected between 1989 and 2009 to assess changes in soil properties, vegetation cover, and crop performance under the impact of aero-technogenic emissions (Vakal & Didukh, 1991, 1992; Vakal & Moskalenko, 1997; Vakal & Golubtsova, 2003; Vakal & Poroshina, 2010).

1.1 Study Profile Characteristics

PJSC "Sumykhimprom" is located on the southeastern outskirts of Sumy city and specializes in the production of phosphate fertilizers, titanium dioxide, defluorinated phosphates, and other products (Trunova, 2006; Trunova & Andriienko, 2003). The main pollutants emitted by the chemical plant are sulfur dioxide (SO_2), hydrogen fluoride (HF), sulfuric acid (H_2SO_4), and nitrogen oxides. Maximum concentrations of these pollutants in the atmosphere are recorded within 0–1000 m from the plant. To assess the scale of ecosystem transformation under the influence of PJSC "Sumykhimprom" emissions, two research profiles were established-eastern (hereafter E) and southeastern (SE) – with a total length of 10 km.

The profiles were aligned according to long-term average wind directions (Figure 1). The eastern profile extends from the reference point through the village of Bezdryk to Zaliznyak, while the southeastern profile passes through the village of Verkhnia Syrovatka. In most cases, northwestern and western winds dominate (up to 56% annually, and up to 80% in summer), resulting in the transport of pollutants primarily toward the SE and E directions from the plant. The profiles start in the immediate vicinity of the PJSC "Sumykhimprom" production area (the reference point is located 25 m from the plant fence).

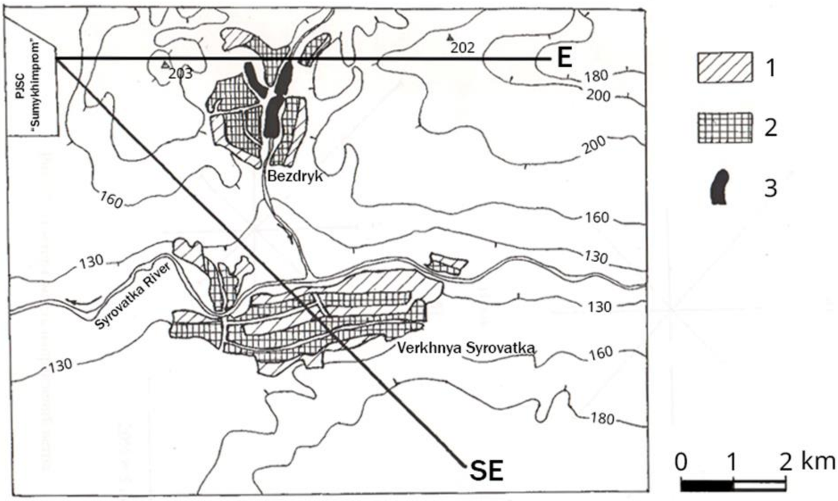

Figure 1. Topographic layout of the research area with designated profiles: 1 – gardens, 2 – residential areas, 3 – water bodies. E – eastern profile through Bezdrik; SE – southeastern profile through Verkhnia Syrovatka.

It is known that the normal pH of precipitation is generally 6.0–6.5. Studies conducted in the area between 1989 and 2003 (Vakal & Didukh, 1992; Tyuleneva & Vakal, 2006) showed that, in most cases, the pH of rainwater decreased from 6.0–6.5 to 5.0–5.2, and in certain periods even to 4.4–4.5. The highest acidity values occur at sites closest to the pollution source (0–1000 m), while at distances of 8–10 km, precipitation acidity decreases to weakly acidic, and in some cases to neutral levels.

In the immediate vicinity of the plant, on the lower parts of the west-facing slope, typical deep, low-humus chernozems occur, with carbonates found only in the parent material. Higher up the slope, in the middle and upper sections, soils of the same type exhibit a shortened profile (horizon thickness H + HR of 60–70 cm), indicating partial erosion of the upper humus layer. The profile then crosses wide watershed plateaus (dividing the basins of the Psel and Syrovatka rivers), dominated by typical deep, low-humus chernozems. In areas formerly covered by oak forests, these soils transition to leached chernozems and dark gray leached soils, which on some relatively small sites are intermixed with sod-podzolic clay-sandy soils (Vakal & Didukh, 1991; Polskyi, 1996).

Along the southeastern direction, the floodplain of the Syrovatka River is sharply distinguished, where meadow-marsh and peat-marsh soils form a complex mosaic. The left bank of the Syrovatka River within the southeastern profile is characterized by typical deep, low-humus chernozems. Parallel studies of soil physico-chemical properties within the area influenced by industrial emissions from PJSC "Sumykhimprom" revealed significant changes in soil structure and chemical composition (Vakal & Didukh, 1992; Vakal & Poroshina, 2010; Kasyanenko & Matsak, 2022).

1.2 Sampling and Assessment of Natural Phytocenosis Disturbance

To assess the degree of disturbance in forest phytocenoses, ten experimental plots (25 × 25 m each) were established along the 10 km-long ecological profiles. Control plots were located 20 km away from PJSC "Sumykhimprom" under conditions similar to those of the experimental sites (Vakal & Didukh, 1991, 1992; Vakal & Golubtsova, 2003).

Both experimental and control plots were placed in undisturbed stands, without signs of logging, windthrow, or other mechanical disturbances, and in areas free from grazing and haymaking. This ensured that the plots retained a natural phytocenotic structure.

To evaluate the nature and intensity of the impact of PJSC "Sumykhimprom" air emissions on soil physical properties, soil samples were collected at varying distances from the pollution source at 500 m intervals throughout the growing season. Samples were taken in triplicate from the arable layer (0–25 cm). The collected soils were analyzed for bulk density, structure, and water stability of the soil aggregates (Lisoval, 2001; Hrytsaienko et al., 2003).

1.3. Methods for Assessing Crop Yield and Quality

Standard methods were applied to determine the yield and quality of winter wheat (Hrytsaienko et al., 2003; Gawęda & Haliniarz, 2021; Grzebisz et al., 2023; Feng et al. 2024). Standard methods for determining yield typically involve harvesting experimental plots at full maturity, followed by threshing, cleaning, and weighing, to calculate yield per hectare.

Sampling was conducted along the ecological profiles over a 10 km distance, at experimental points spaced every 500 m. In each sampling point, plants were collected from 10 plots, each measuring 1 m^2.

Key yield components were assessed, including: plant density (per 1 m^2), total and productive tillering, spike length, number of spikelets per spike, grain number and weight per spike, and 1000- grain weight.

To evaluate crop structure, plants from the 1 m^2 plots were uprooted and combined into a single bundle. For each bundle, the total number of plants, total tillers (all stems), and productive tillers (stems bearing spikes) were recorded. Plant height was measured on 25 randomly selected plants, from the base of the tiller node to the tip of the main spike, excluding awns. Roots were removed, and the bundle was weighed. Spike length was measured from the base of the first spikelet to the base of the uppermost spikelet. The number of spikelets per spike was counted, including underdeveloped ones in the lower part. Twenty-five consecutive spikes were then analyzed to determine average spike length, spikelets per spike, and grain weight per spike (grain weight was calculated as total weight of 25 spikes divided by number of grains).

The bundles were threshed, and grain weight was recorded together with grains from the 25 spikes. The 1000-grain weight was determined using two consecutive samples of 1000 grains each, weighed to the nearest 0.01 g. If the difference between the two samples exceeded 3%, a third sample was measured, and the 1000-grain weight was calculated as the mean of the two most consistent samples.

Grain and straw chemical composition of winter wheat grown in the industrially polluted zone was analyzed at Astra Laboratories LLC (Sumy, Ukraine).

2. Results and Discussion

Industrial aero-technogenic emissions, particularly sulfur dioxide (SO_2) and hydrogen fluoride (HF), exert notable pressure on both natural and agro-ecosystems in the immediate vicinity of PJSC “Sumykhimprom”. The studies conducted in 2023 allowed us to assess the current state of soils, vegetation cover, and winter wheat yield and to compare these findings with historical data dating back to 1989.

The following subsections present detailed results on: (i) changes in soil physical properties, (ii) transformations in vegetation cover, and (iii) impacts on winter wheat productivity and grain quality within the influence zone of industrial emissions.

2.1. Soil Physical Property Changes under Aero-Technogenic Emissions

The properties of soils are shaped by the intensity and direction of the processes underlying their genesis and represent the combined effect of soil-forming factors. Increasing anthropogenic impact alters soil properties, their functional characteristics, and the course of pedogenic processes. Such changes may be local, specific to a particular soil type, or regional in scale, and ultimately can lead to serious consequences, including the loss of fertility (Malysheva, 1997; Makarenko et al., 1999).

As chernozems and dark gray podzolic soils are the most valuable for agricultural use within the studied area, particular attention was given to changes in the physical properties of these soil types. Agricultural use of the soils, combined with the influence of industrial emissions from PJSC "Sumykhimprom," has driven the transformation of their physical characteristics, particularly agronomically important parameters such as soil structure, bulk density, and aggregate stability.

The structural-aggregate composition of the arable layer in soils within the zone of intensive pollution has undergone substantial changes compared to soils located more than 3 km from PJSC "Sumykhimprom" and to control samples. In these soils, there is an increase in coarse clod aggregates, a reduction in fine particles, a decrease in the proportion of agronomically optimal-size aggregates, and a deterioration in the water stability of the soil structure (Table 1).

Table 1. Soil bulk density and structural composition in the research area

Distance from the pollution source, km	Bulk density, g/cm³	Structural composition, %				Water stability coefficient
		Aggregate size, mm				
		10	10-0,25	0,25	Structural coefficient	
0	1,52	70	29	1	0,4	0,2
E profile						
1	1,43	46	50	4	1,0	0,3
2	1,36	33	63	4	1,7	0,3
3	1,28	22	75	3	3,0	0,4
4	1,22	23	73	4	2,7	0,4
8	1,26	18	76	6	3,2	0,5
9	1,29	16	77	7	3,3	0,5
10	1,31	21	73	6	2,7	0,5
SE profile						
1	1,37	39	59	2	1,4	0,3
2	1,42	40	57	3	1,4	0,3
3	1,31	20	78	2	3,5	0,4
6	1,23	19	76	5	3,2	0,4
7	1,25	16	74	8	2,8	0,5
8	1,25	20	73	7	2,7	0,4
9	1,19	18	77	5	3,3	0,4

Agronomically valuable soil fractions are represented by soil aggregates ranging in size from 0.25 to 10 mm (Danylova, 1996; Hillel, 2004). In soils located in the immediate vicinity of the pollution source, their content decreases to 29–50%, while the proportion of cloddy aggregates reaches 40–70%. On plots situated 6–10 km from the chemical plant, the proportion of cloddy aggregates decreases to 16–20%, whereas the content of agronomically valuable aggregates (0.25–10 mm) increases to 73–78%, which is characteristic for soils of these types (Kovalov et al., 2022).

Approaching the chemical plant (0–2 km), the structural coefficient declines from 2.7–3.3 (typical for soils located beyond 3 km from PJSC "Sumykhimprom") to 0.4–1.4, indicating a significant deterioration of the structural composition of soils in the study area (Table 1).

An important parameter is also the soil's ability to retain a plant-favorable structure over time, which can be evaluated using the water-stability coefficient of soil aggregates.

Studies carried out for this purpose showed that the water-stability coefficient decreases from 0.4–0.5 (typical for soils at 8–10 km from PJSC "Sumykhimprom") to 0.2–0.3 in soils located 0–2 km from the chemical plant (Table 1).

The deterioration of the structural–aggregate composition of soils located within the zone of intensive atmospheric pollution (0–2 km from the plant) consequently leads to an increase in the bulk density of the arable layer (Table 1).

Soil structure typically degrades when natural vegetation is removed and soils are intensively cultivated (Danylova, 1996; Bronick & Lal, 2005). However, since plots at varying distances from PJSC "Sumykhimprom" are subject to practically the same intensity of agricultural management, the observed deterioration of the structural–aggregate composition and the increase in soil bulk density on plots within 3 km of the chemical plant can be attributed to the impact of aero-technogenic pollution.

A comparative analysis of the results obtained with data from 1989 (Vakal & Didukh, 1991, 1992; Vakal & Poroshina, 2010) indicates that the main physical properties of soils within the zone of influence of PJSC "Sumykhimprom" air emissions have remained largely unchanged. Soil bulk density, structural coefficients, and water stability showed no significant variations, while on some plots (0–0.5 km from the chemical plant) these parameters even improved from an agronomic perspective. Structural coefficients increased from 0.3 to 0.4–0.7, and water stability of soil aggregates increased from 0.15 to 0.2–0.3, which is associated with a reduction in the proportion of soil aggregates larger than 10 mm in this area.

Soil analyses demonstrate that soils within the emission impact zone of PJSC "Sumykhimprom" have undergone substantial changes in their physical properties compared to control plots. Although the volume of aero-technogenic emissions has decreased over the past twenty years, there has been practically no improvement in the physical properties of soils affected by air pollution, indicating only a certain stabilization of ongoing soil processes.

2.2. Vegetation Cover Transformation in Response to Aero-Technogenic Emissions

To assess the degree of disturbance in forest biocenoses under the influence of pollution, the primary criteria considered were the condition of the ground vegetation and the stand structure. The assessment of forest biocenosis disturbance was conducted along the direction of the ecological profile over a distance of 10 km on 10 sample plots, and results were compared with control plots located 20 km from PJSC "Sumykhimprom" (Vakal & Didukh, 1991, 1992; Vakal & Moskalenko, 1997).

The stability of forest stands is largely determined by their structure, species composition, and age. When studying the effects of SO_2 and HF on forest phytocenoses, initial attention was focused on the condition of the stand. Notably, the onset of dieback was observed in certain trees, primarily in oak stands. In forest plots located in close proximity to PJSC "Sumykhimprom" (0.5–3.5 km), the stand was dominated by Quercus robur L., with Acer platanoides L. as a co-dominant. However, in some associations, A. platanoides began to assume a dominant position. The impact of anthropogenic factors, coupled with differences in species competitive ability (Vakal & Moskalenko, 1997), led to a gradual increase in the phytocoenotic role of A. platanoides and a decrease in that of Q. robur. Most Q. robur individuals exhibited dry lateral branches, strongly thinned crowns, and the development of tip dieback.

According to the literature (Prysedskyi, 2003, 2014), excessive accumulation of sulfur in plants leads to the appearance of necrotic damage. In our observations, widespread necrosis of the leaves of Quercus robur and Acer platanoides was noted on sample plots located 500–700 m from the chemical plant, as well as in Populus nigra var. pyramidalis Spach. and Morus alba L., at distances of 100–500 m from PJSC "Sumykhimprom." The damage symptoms primarily manifested in young leaves that had not yet fully unfolded.

It should be noted that from the 1990s to the present, a significant decline in the number of Morus alba individuals has been observed, and within 300 m from the pollution source, most of the trees have perished (Vakal & Didukh, 1991, 1992; Vakal & Moskalenko, 1997).

The species most resistant to aero-technogenic pollution on these plots are Populus nigra L. and Fraxinus excelsior L.; however, by the end of the growing season, widespread leaf necrosis was also observed in these trees.

On all sample plots, suppressed leaf development was also recorded in Acer negundo L., while the leaves of Euonymus europaeus L. showed no damage to the leaf blades.

Previous studies of the floristic composition of the ground vegetation revealed significant changes with proximity to the chemical plant. On the control plots, associations such as Quercetum asaroso-aegopodiosum and Quercetum asaroso-stellariosum predominated, while Quercetum urticosum was observed only in depressions. Near PJSC “Sumykhimprom,” however, Quercetum urticosum and Acereto-Quercetum asaroso-urticosum associations occupy large areas on the slopes.

On all plots located more than 4 km from the source of aero-technogenic pollution, forest species predominate. With closer proximity to PJSC “Sumykhimprom,” the herbaceous layer shows a replacement of forest vegetation by ruderal species. Typical forest species such as Aegopodium podagraria L. and Stellaria holostea L. are largely displaced, and Urtica dioica L. and Asarum europaeum L. dominate the herbaceous layer. Occasional occurrences of A. podagraria, S. holostea, Lamium purpurea L., and Geum urbanum L. are recorded with a projected cover of 4–5%. The presence of Urtica dioica on slope plots in close proximity to the chemical plant is explained by its highly competitive ability compared to other forest herbaceous species. In zones with high concentrations of SO_2 and HF in the air, Dryopteris filix-mas (L.) Schott is completely absent.

The data obtained in 2023, in comparison with previous studies (Vakal & Didukh, 1991, 1992; Vakal & Moskalenko, 1997), indicate that in recent years, on plots located in close proximity to PJSC “Sumykhimprom” (0.5–2.0 km), there has been a partial restoration of the species composition of the herbaceous layer typical of oak forests. Specifically, within the projected cover of Quercetum urticosum and Acereto-Quercetum asaroso-urticosum associations, the abundance of ruderal species such as Urtica dioica and Chelidonium majus has decreased, while the presence of Aegopodium podagraria and Stellaria holostea has increased.

2.3. Impact of Aero-Technogenic Emissions on Winter Wheat Yield and Grain Quality Traits

The problem of studying the impact of aero-technogenic emissions on the yield of agricultural crops is of great importance for Ukraine, since its territory hosts vast areas of high-quality agricultural land. However, the development of the chemical, metallurgical, and energy industries in our country has led to the accumulation of large amounts of pollutants in the atmosphere, which significantly affect the quality of agricultural lands and reduce their productivity (Malysheva, 1997; Makarenko et al., 1999; Moldavan et al., 2023).

A number of studies provide data on the effects of air emissions on the condition and yield quality of agricultural crops, but most of them were obtained either under laboratory conditions or for other agro-climatic zones (Sun et al., 2017; Fedoniuk et al., 2019). Among all types of pollutants, the consequences of sulfur, fluorine, and certain other compounds are the best studied. In most cases, elevated concentrations of SO_2 and HF in both air and soils, according to many authors, negatively affect plant development, causing significant damage to leaf tissues and altering several physiological and biochemical processes.

The objective of our study was to determine the extent of the impact of atmospheric emissions from PJSC Sumykhimprom on the yield and quality of winter wheat. This issue is of particular relevance for the region, as winter wheat is the country's leading grain crop. The research was conducted during 2023 on the lands of the Verkhnio-Syrovatka, Bezdrivka, and Sumy territorial communities.

Meteorological conditions during the vegetation period of winter wheat (2022–2023) were favorable for plant growth, ripening, and harvesting. For agricultural enterprises of this region, the characteristic cropping system is an eight-field grain crop rotation, with cereals accounting for up to 55–60%, legumes up to 15%, oil crops up to 15%, and clover 10–15%. The principal scheme of this crop rotation is as follows: field 1 – winter wheat; field 2 – maize for grain; field 3 – sunflower; field 4 – soybean; field 5 – winter wheat; field 6 – maize for grain; field 7 – barley undersown with grasses; field 8 – perennial grasses (Vakal & Lytvynenko, 2021).

This study examines the effects of SO_2 and HF on the yield and quality of winter wheat (Triticum aestivum L.). The experiments were carried out in 2023 on plantings of the locally adapted winter wheat varieties Okhtyrchanka, Yuvileyna, and Vozdvyzhenka, grown on typical low-humus chernozem and dark gray forest soils. Winter wheat was placed in the crop rotation according to the accepted alternation after perennial grasses and soybean.

The cultivation technology of winter wheat included the following practices. After fallow and with the application of organic fertilizers, plowing was carried out to a depth of 22–24 cm, simultaneously preparing the soil for pre-sowing conditions. After non-fallow predecessors (peas), a moisture-preserving tillage technology was applied at a depth of 10–12 cm. To ensure uniform growth and development of plants across the field, leveling of the soil with simultaneous harrowing was performed after the primary tillage. Prior to sowing, the field underwent continuous cultivation to the depth of seed embedding. Wheat was sown in a solid seeding method from September 1 to 5 (Vakal & Lytvynenko, 2021).

The seeding rate of winter wheat was 4.5–5.0 million viable grains per hectare. The seeding depth was 5–6 cm. Immediately after sowing, rolling was performed with ring-spike rollers. In spring, the crops were harrowed in two passes using light harrows. Harvesting was carried out by the two-phase harvesting method.

The fertilizer system for wheat included the basic application of the entire dose of phosphorus (40 kg/ha) and potassium (60 kg/ha) fertilizers, pre-sowing application of 10 kg/ha phosphorus, and nitrogen fertilization during the spring-summer period. The first application (30 kg/ha N) was carried out at the tillering stage when the soil reached physical maturity, using band application. The second nitrogen fertilization (40 kg/ha N) was performed at the stem elongation stage.

The results of the conducted research demonstrated that industrial air emissions accelerate the ripening of wheat crops. Thus, full grain maturity in fields located near the source of pollution (within 1.0 km) occurred on average 5 days earlier compared to more distant plots (9–10 km).

In the zone of aero-technogenic pollution, the average plant height changed significantly (Table 2).

For the closest plots, it averaged 68.1 cm, which is approximately 9–9.5 cm lower than that of plants sampled 9–10 km away from the emission source. A decrease in yield was also observed, caused by a reduction in the number of productive tillers per 1 m², the average ear weight, and the weight of 1,000 grains.

Table 2. Grain and straw yield of winter wheat and its quality indicators in the zone of influence of air emissions (2023)

Distance from the pollution source, km	Yield, q/ha		1000-grain weight, g	Average grain weight per spike, g	Productive tillers, plants/m²	Plant height, cm
	Grain	Straw				
0,5–1,0	39,2±1,5	39,5±3,2	40,08±1,2	0,97±0,05	304±9	71,9±4,8
2,0–2,5	44,3±1,7	45,9±3,8	40,68±1,4	1,02±0,06	324±10	70,6±5,1
3,5–4,0	51,6±2,1	48,8±4,9	41,27±1,3	1,09±0,09	371±10	76,3±5,0
9,0–10,0	56,5±2,7	51,7±5,1	41,42±1,2	1,18±0,08	381±11	77,9±4,9

High atmospheric pollutant concentrations were found to exert an adverse influence on the formation of productive tillers. Under the optimal seeding density of 4.5–4.7 million viable seeds per hectare, the number of productive tillers in wheat stands located in close proximity to chemical plants (≤1.0 km) amounted to 304–310 tillers m^{-2}, whereas at distances of 9–10 km it increased to 375–385 tillers m^{-2}.

Grain harvested from more remote fields, where the influence of industrial emissions was negligible, was characterized by more favorable physical properties, including greater grain plumpness and a higher proportion of large-sized grains (up to 85%). In parallel, the mean thousand-grain weight exhibited a consistent increase with distance from the emission source, ranging from 40.08 to 41.42 g. A comparable trend was recorded for grain weight per spike: the mean spike mass of winter wheat rose from 0.97 g at sites adjacent to chemical plants to 1.18 g at more distant sites.

The total yield of grain and straw on plots located within 1.0 km from PJSC Sumykhimprom amounted to 78.7 c/ha.

On plots situated at a distance of 3.5 to 10.0 km, the overall yield of winter wheat was higher, reaching 100.4–107.2 c/ha. The difference in total yield between the nearest and the farthest plots ranged from 22.7 to 28.5 c/ha in favor of the latter.

A similar trend was observed for grain yield alone. Thus, on plots located within 1.0 km from the pollution source, the grain yield was 39.2 c/ha, whereas on distant plots (9–10 km) it reached 56.5 c/ha.

As can be seen, a significant decrease in winter wheat productivity is observed in the immediate vicinity of the atmospheric pollution source, where the yield values are approximately 1.5 times lower compared to plots situated more than 3.5 km away from the chemical plants.

In parallel with the assessment of winter wheat yield, the chemical composition of its grain and straw was also studied (Table 3). The data obtained indicate that, as proximity to PJSC Sumykhimprom increases, the fat content in the grain rises from 2.12% at 9–10 km to 2.25% at 0.5–1.0 km, whereas the crude protein content decreases from 12.27% to 11.04% over the same distance. No clear relationship was observed between the percentage of fiber in the grain and the concentration of atmospheric pollutants. Similarly, the contents of calcium, potassium, phosphorus, and ash in the winter wheat grain did not show any dependence on the distance from the pollution source.

Table 3. Chemical composition of winter wheat grain and straw in the zone of industrial pollution influence (2023)

Distance from the pollution source, km	Crude protein	Chemical composition, %						Soluble fluoride, mg/kg	SO_4^{2-}, mg/kg
		Fat	Fiber	Ca	K	P	Ash		
Grain									
0,5–1,0	12,04	2,25	3,14	0,28	0,53	0,51	2,27	1,78	89.6
2,0–2,5	12,19	2,12	3,08	0,27	0,53	0,50	2,23	1,52	87,3
3,5–4,0	12,28	2,09	3,11	0,29	0,51	0,49	2,24	1,27	84,1
9,0–10,0	12,27	2,12	3,14	0,27	0,52	0,50	2,20	0,74	75,9
Straw									
0,5–1,0	4,17	1,32	43,27	0,75	1,26	0,24	5,97	52,61	395,5
2,0–2,5	4,16	1,32	43,34	0,79	1,30	0,25	6,09	29,2	357,8
3,5–4,0	4,31	1,30	43,48	0,77	1,33	0,23	6,11	20,42	302,1
9,0–10,0	4,39	1,31	43,76	0,81	1,41	0,24	6,29	5,48	279,4

In the straw, increasing distance from the chemical plant was associated with an increase in crude protein content from 4.17% (0.5–1.0 km) to 4.39% (9–10 km), fiber from 43.27% to 44.38%, calcium from 0.75% to 0.81%, potassium from 1.26% to 1.41%, and ash from 5.97% to 6.29%. No pronounced variation in calcium and phosphorus content in the straw was observed in relation to the concentration of atmospheric pollutants.

Conversely, approaching the pollution source led to an increase in water-soluble fluoride and sulfate ions in both grain and straw. In the straw, the content of water-soluble fluoride increased from 5.48 mg/kg (at 9–10 km from the chemical plant) to 52.61 mg/kg (at 0.5–1.0 km), while sulfate ions rose from 279.4 to 395.5 mg/kg, respectively, on a completely dry matter basis.

Thus, the study of the chemical composition of wheat grain and straw demonstrated that high concentrations of sulfur dioxide and hydrogen fluoride in the air and soil during the plant growth period led to more pronounced changes in the chemical composition of straw compared to that of the grain.

In addition, in the zone influenced by the chemical plant, necrotic lesions were observed on the leaves of winter wheat.

The direct impact of industrial air emissions, combined with alterations in the physicochemical properties of soils, resulted in increased weed occurrence in winter wheat fields located in the immediate vicinity of the chemical plant. Among the weeds, the most pollution-tolerant species, perforate or scentless chamomile (Matricaria perforata Mérat) and cornflower (Centaurea cyanus (All.) Dost.), were abundant. With increasing distance from the pollution source, the species diversity of weeds increased, whereas their projected cover decreased.

Based on the degree of transformation of winter wheat yield and its quality parameters, previous studies (Vakal & Didukh, 1991, 1992; Vakal & Moskalenko, 1997; Vakal & Golubtsova, 2003; Vakal & Poroshina, 2010) have delineated four zones, the boundaries of which have remained virtually unchanged over the past thirty years, as confirmed by our research (Vakal & Lytvynenko, 2024):

a) Intensively polluted zone (up to 1.5 km from the chemical plant). In this zone, the winter wheat yield is approximately half that of the control. The content of water-soluble fluoride in grain and straw exceeds background levels. Reductions were observed in the thousand-grain weight, average grain weight per spike, number of productive tillers per square meter, and plant height.

b) Moderately polluted zone (from 1.5 to 3.5–4 km from the chemical enterprises). Compared with the intensively polluted zone, winter wheat yield and quality parameters in this zone are higher and better, although in some cases the content of water-soluble fluoride in grain and straw still exceeds background levels.

c) Weakly polluted zone (from 3.5 to 10 km). Winter wheat yield and quality parameters do not differ from those of the control plots. The content of water-soluble fluoride in plants does not exceed the maximum permissible concentration.

d) Practically clean zone (10–12 km and beyond). The content of water-soluble fluoride in plants does not exceed background levels.

CONCLUSIONS

Air emissions (SO_2 and HF) from PJSC Sumykhimprom exert a pronounced negative impact on natural and cultivated plant communities, particularly within the intensive pollution zone (up to 1.5 km from the source). In this zone, plant cover undergoes transformation: species sensitive to pollutants disappear, while associations such as Quercetum urticosum and Acereto-Quercetum asaroso-urticosum occupy large areas, displacing species typical of oak forests, notably Aegopodium podagraria and Stellaria holostea. The most resistant woody and shrub species to emissions were found to be Populus nigra, Fraxinus excelsior, and Euonymus europaea, whereas Acer platanoides and Quercus robur show visible damage (leaf necrosis, growth suppression). Morus alba has nearly disappeared within a 300 m radius of the plant.

A comparison of recent findings with data from the 1990s–2000s indicates partial recovery of the herbaceous layer in oak forests within 0.5–2.0 km of the emission source. In the projective cover of Quercetum urticosum and Acereto-Quercetum asaroso-urticosum, the proportion of ruderal species (notably Chelidonium majus) has declined, while the shares of Aegopodium podagraria and Stellaria holostea have increased.

Soil studies revealed substantial alterations in their physical properties within the impact zone compared to control plots. Despite a reduction in aero-technogenic emissions over the past twenty years, no significant improvement in soil properties has been observed; only a certain stabilization of degradation processes can be noted.

In agroecosystems, the negative influence is manifested by a reduction in winter wheat yield by approximately 1.5 times compared to control plots, caused by decreases in 1000-grain weight, average grain weight per spike, and the number of productive tillers. Crop maturation occurred, on average, five days earlier in close proximity to the plant. Grain quality also declined: contents of water-soluble fluorine and sulfate ions were higher, with even more pronounced differences observed in straw.

Changes were also recorded in the contents of fat, crude protein, fiber, calcium, potassium, and ash, with straw showing stronger chemical alterations than grain.

Additionally, wheat crops located near the emission source exhibited an increased abundance of weeds, particularly Matricaria perforata and Centaurea cyanus. With increasing distance from the plant, species richness of weeds rose, but their projective cover decreased.

In summary, based on the transformation of natural and agroecosystems and the observed changes in wheat yield and quality, the division of the territory into four stable zones of aero-technogenic impact is confirmed. The boundaries of these zones have remained nearly unchanged for more than 30 years: intensive pollution zone (up to 1.5 km), moderate pollution zone (1.5–3.5–4 km), weak pollution zone (3.5–10–12 km), and practically clean zone (beyond 10–12 km).

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CHAPTER 3
ENHANCING PREDICTIVE ACCURACY AND GENERALIZABILITY IN SOCIO-ENVIRONMENTAL SYSTEMS THROUGH HYPERPARAMETER OPTIMIZATION

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INTRODUCTION

The intricate interplay between human activities and the environment necessitates a profound understanding of ecological systems, climate patterns, and the impact of human actions on the planet. As a result, environmental data has emerged as a critical tool for informed decision-making and the pursuit of sustainable practices. Socio-environmental systems involve the complex interaction among human (i.e., social, economic) and natural (i.e., biophysical, ecological, environmental) systems (Elsawah et al., 2020). The concern for environmental quality is pervasive worldwide, impacting both developed and developing nations (Miller, 2021; Milosevic et al., 2023).

For decades, the issue of energy use, access, choice, and management has been central to global discourse, not only due to its socioeconomic role in industrial development but also because of its profound impact on human health and environmental footprints across regions. The development and use of clean energy are now at the forefront of the climate change discourse, intricately linked to economic growth and productivity within the sustainable development agenda (Chen et al., 2023; Furtado et al., 2023).

Recent studies have contributed valuable insights into the driving forces of energy-related carbon emissions, exploring the mechanisms by which anthropogenic factors shape environmental outcomes. Various models have been developed to examine these mechanisms, with the STIRPAT (Stochastic Impact by Regression on Population, Affluence, and Technology) model emerging as a widely applied approach (Dietz and Rosa, 1997; McGee et al., 2015; Wu et al., 2021; Nasrollahi et al., 2018; Li et al., 2015; Aderinto, 2022; Aboyitungiye & Suryanto, 2021; Balcilar et al., 2023; Wang et al., 2021).

The STIRPAT framework, a reformulation of the IPAT model (Impact = Population × Affluence × Technology), introduced stochastic elements allowing for greater flexibility in testing assumptions and empirical estimation (Dietz and Rosa, 1997). Its application has provided critical insights into the environmental impacts of population growth, technological advancements, and economic affluence.

However, despite its widespread use, the STIRPAT model often encounters practical challenges, particularly related to the complexity of environmental datasets.

These datasets frequently exhibit multicollinearity and other intricate relationships that traditional regression techniques, such as Ordinary Least Squares (OLS), struggle to handle effectively. OLS is prone to overfitting and poor generalization when dealing with correlated variables, leading to suboptimal predictions (Li et al., 2015; Nilashi et al., 2023; Subramanian & Simon, 2013).

In response to these challenges, more sophisticated methods, such as Partial Least Squares (PLS), have been developed (Li et al., 2021; Chekouri et al., 2020). These techniques offer improved handling of multicollinearity by capturing latent variables and ensuring more robust generalization. By projecting both the predictor and response variables into a new space, PLS helps mitigate the limitations of traditional regression, allowing for more accurate environmental modeling.

Moreover, the regularization introduced in ROPLS adds an extra layer of refinement, controlling for overfitting by penalizing model complexity. Using orthogonal components in ROPLS allows the model to account for variations in predictors uncorrelated with the response, thus further improving model performance and interpretability.

Another critical factor in enhancing model performance is optimizing hyperparameters (Kohavi and John, 1995), a technique that systematically tunes model parameters to achieve the best possible outcomes (Mantovani et al., 2016; Olson et al., 2018). By refining parameters such as the number of latent variables or the strength of regularization, hyperparameter optimization helps ensure that models strike the right balance between complexity and generalizability. Techniques such as grid search and Bayesian optimization are commonly used to explore the optimal parameter space, providing more accurate and robust predictions of environmental impacts (Mantovani et al., 2016; Olson et al., 2018).

While previous studies have applied the STIRPAT model to investigate the relationship between anthropogenic activities and environmental degradation, many have relied on traditional regression techniques like OLS, which are vulnerable to issues such as multicollinearity and overfitting.

Although some studies have explored the use of PLS and ROPLS, the application of hyperparameter optimization in conjunction with these advanced techniques has not been fully explored.

Additionally, the potential of ROPLS to handle the complex dynamics of environmental datasets remains underutilized, particularly in the context of systematic tuning for improved predictions.

This paper aims to bridge this gap by exploring the application of OLS, PLS, and ROPLS in conjunction with hyperparameter optimization to enhance the predictive performance of the STIRPAT model in environmental analysis. By comparing these methods and systematically tuning key parameters, this study demonstrates how advanced techniques can yield more accurate forecasts of socio-environmental systems, offering valuable insights for researchers and policymakers alike. This research contributes to the field of environmental modelling by addressing the limitations of traditional regression techniques and demonstrating the effectiveness of advanced methodologies in enhancing model performance. The integration of hyperparameter optimization with PLS and ROPLS provides a novel approach to forecasting environmental impacts, potentially offering more reliable tools for tackling the challenges of climate change and sustainable development.

1. Methodology

1.1 Data Source

Time series data from 2000-2020 from Nigeria were used for the study. The data were sourced from various national and international databases that were reliable for the study. The study involves the direct use of variables and where variables cannot be found a proxy was introduced to represent the variable. The table below summarizes the description and sources of the data.

For the study, solid biofuels were used as a proxy for environmental impact due to their major social and ecological role (Lambe et. al., 2015) while electricity access as a moderator variable to clean cooking access to represent fuel staking and the role played by renewable energy sources on environment and energy use (Sibanda et al., 2024; Owusu and Asumadu-Sarkodie, 2016; Ritchie et al., 2024).

To understand variations in the population the STIRPAT model was extended to include agricultural dynamics to make a good representation of the population due to the role played by agriculture in income earning and rural development and the correlation between energy security, income, and sustainability (Baiyegunhi and Hassan, 2014; Raihan et. al., 2023a; Raihan et. al., 2023b).

Table. 1 Description of variable in the study

Symbol	**Variable**	**Definition**	**Unit of Measurement**	**Source**
Solid_Impact	Solid biofuels	This is the total amount of Firewood, charcoal, and agricultural residues used	Million ton of oil equivalent (MTOE)	IEA-SBE MODEL, (2022)
P	Population size	This is the total number of male and female population in Nigeria	Million	(World Bank Open Data 2024)
ATFP	Agricultural Total Factor Productivity	Agricultural total factor productivity, (TFP) measures the efficiency and productivity of all inputs used in agriculture, including labor, land, and capital, in producing agricultural output.	_	USDA-ERS (2023)
perCGDI	Per capita Gross Domestic Income	This is the county's economic output per person in a Year	Constant 2017 International Dollar prices ($)	(World Bank Open Data 2024)
NCCA	Non-access to clean cooking	This is the total number of populations without clean cooking	Million	Ritchie *et al.* (2024)
ECCESS	Access to electricity	This is the total number of populations with electricity access	Million	Ritchie *et al.* (2024)

In this analysis, the dataset was restricted to the period from 2000 to 2020. Data for 2021, 2022, and 2023 were not included due to the absence of real observations for these years in some of the variables. Replacing the missing values with mean estimates would have introduced artificial trends, leading to potential distortions in the model, especially during differencing. Therefore, to maintain the integrity of the analysis and ensure reliable results, the study was limited to the available data up to 2020.

1.2 Analytical Techniques and Model Development

1.2.1 Stationarity Test

To satisfy most statistical model's key assumptions and arrive at more reliable and interpretable results, the usual first step in time series analysis is to determine the degree of integration of each variable.

A fundamental purpose of using a unit root test is to control whether or not each time-series data contains a unit root (Dogan and Ozturk, 2017). Hence, all series were tested for non-stationarity using the Kwiatkowski-Phillips-Schmidt-Shin (KPSS). Using the default 5% significance level all the series were tested before the analysis using R-studio (V.4.4.0). The general equation for the test is given by:

KPSS=1/T2 ∑_(t=1)^T▒〖S2 t〗 Kwiatkowski et. al., (1992)

where St is the sum of residuals from a regression of yt on t, and T is the number of observations.

Based on the decision-making criteria of KPSS, if the p-value is less than the significance level at 5%, we fail to reject the Null hypothesis that the series were stationary (Kwiatkowski et. al., 1992). Therefore, it implies that these series do not exhibit unit root behavior and are stable over time.

1.2.2 Cointegration Analysis

The Johansen (Johansen, 1991) method allows for all possible co-integrating relationships and the number of co-integrating vectors to be determined empirically (Johansen & Juselius, 1990. Applying the cointegration test is very important because this procedure allows the research to examine the relationships between the variables. The existence of cointegration indicates a balance between the model's variables in the long run. Johansen's cointegration test implies the estimation of an autoregressive vector model, known as VAR, including values at levels as well as differences of non-stationary variables. At this stage, a VAR model is configured to determine the optimal lag length, and the SIC - Schwarz information criterion is applied to optimize lag lengths for the time series. The Johansen test equation is described as follows:

dXt = 1 dXt=1 + ………. k=1 dXt=k+1 πXt=K + Ɛ where E is the random variable, pi and pie demonstrate the OLS parameter matrices, piXt=K examine the linear combinations of levels of Xt and the matrix pi has the information about properties. The literature mentions two statistics determining the degree of the matrix coefficient or the numbe rof cointegration relationships. Thess statistics are obtained through the use of two likelihood (LR) tests- the trace statistics and the max-eigen statistic whose application examines the null hypothesis on the number of cointegration ratios r versus the alternative hypothesis r+1.

The presence of cointegration is required for applying regression methods using PLS and ROPLS models. Therefore, based on trace statistics and max-eigen statistics the rejection of the null hypothesis is necessary with significance level of 5% for the confirmation of long term cointegration between the model series (Hänninen, 2012).

1.2.3 Model Development

The original STIRPAT model is (Rosa and Dietz, 1998)

I=aP^b A^c T^e

Where; I, P, A, and T have the same implications as in the IPAT framework; a scale the model; b, c, and d are the estimated exponents of P, A, and T, respectively; and e is the error term. When a = b = c = d = e = 1, the IPAT equation can be considered as a special form of the STIRPAT model. To facilitate empirical estimation and hypothesis testing, this model is often converted into logarithmic form: thus;

$$\ln I = a + b(\ln P) + c(\ln A) + d(\ln T) + e$$

Therefore, the extended model for this study is given by;

$$\ln Solid\_Impact_{it} = C + \beta_1 \ln(P_{it}) + \beta_2 \ln(perCGDI)_{it} + \beta_3 \ln(NCCA)_{it} * \beta_4 \ln(ECESS)_{it} + \beta_5 \ln(ATFP)_{it} + \varepsilon_{it}$$

β_1, β_2, β_3, β_4, β_5 in the model are interpreted as ecological elasticities while ε_{it} is the epsilon and stochastic noise

The PLS linear regression model is appropriate for our study due to its ability to control the presence of multicollinearity of variables (Li et al., 2015).

According to the theory of PLS, R2 X denotes the explanatory ability of the principal Components extracted from X variables to the original X variables, R2 Y denotes the explanatory ability of the principal components extracted from Y variables to the original Y variables, and Q2 represents the cross-validation, which measures the marginal contribution of the extracted component to the model precision.

To improve model robustness and interpretability, the research incorporates orthogonal signal correction and regularization to enhance model robustness interpretability a partial least square was run using orthogonal components (1:3) and tuning hyperparameter (0:2) by grid search (Andonie, 2019) with k-5 folds cross-validation. The data is split into training (20%) and testing (80%). The general OPLS model is given by

Y=T_(1) Q^'1 + E

Where:

Y is the response matrix.

T1 is the score matrix of the predictive components.

Q1 is the loading matrix of the predictive components.

T2 is the score matrix of the orthogonal components.

Q2 is the loading matrix of the orthogonal components.

E is the residual matrix.

The step for the estimation were

a) Data Preparation

All the six series were standardized using z-score normalization to ensure they are on the same scale before the analysis to reduce noise and error in computation.

$$Zi = \frac{xi - ui}{\sigma i}$$

Where;

Zi: Normalized value of predictor Xi, response Yi

μi: Mean of predictor Xi, response Yi

sigma_σi: Standard deviation of predictor Xi, response Yi

b)Fitting the OPLS Model

The model decomposes X into orthogonal (predictive) components and Y as follows:

$$X = TP^{\mathrm{T}} + E^{\mathrm{uuu}}$$

$$Y = UQ^{\mathrm{T}} + E$$

Where:

T: Score matrix for X

P: Loading matrix for X

U: Score matrix for Y

Q: Loading matrix for Y

E: Residual matrix for X

F: Residual matrix for Y

The relationship between X and Y can be expressed as:

Y=XB+FY

Where B is the regression coefficient matrix.

b) Variable Importance in Projection Extraction

$$\boldsymbol{VIP} = \sqrt{\frac{\boldsymbol{\rho}}{\sum_{\boldsymbol{k-1}}^{\boldsymbol{A}} \boldsymbol{T_k^T T_k}} \sum_{\boldsymbol{k=1}}^{\boldsymbol{A}} (\boldsymbol{T_k^T\ T_k}) \left(\frac{\boldsymbol{b_k}}{||\boldsymbol{b}||}\right)}$$

Where:

- VIPj score for predictor Xi
- p: Number of predictors
- A: Number of components
- Tk: Scores of the k-th component
- bk: Regression coefficients of the K-th component

1.3 Predictive Accuracy And Generalizability İndicators

To get a balanced view of predictive accuracy and robustness of estimation to assess the performance of the models, several indicators were computed, including Cross-Validation R2, and Q2, which are widely considered for evaluating predictive accuracy and generalizability.

- Cross-Validation: Cross-validated R2 was calculated to measure the model's ability to predict unseen data. This metric reflects the degree of overfitting or underfitting in each model and provides information on how well the model generalizes beyond the training dataset (Kohavi, 1995; Stone, 1974; Browne, 2000; Roberts et al., 2016)
- Explained Variance: The R2 value, representing the proportion of variance explained by the model, was used to evaluate the fit of each model. Higher values indicate better performance in capturing the relationship between predictors and the outcome (Cameron & Windmeijer, 1997; Gelman et al., 2018).
- Predictive Power: Q2 was computed to assess the model's predictive relevance based on cross-validation. A positive value reflects good predictive accuracy, while a negative or lower value indicates poor generalizability and possible overfitting. This metric is particularly important for Partial Least Squares (Chong & Jun, 2005; Triba et al., 2014)

2. Result and Discussion

2.1 Stationarity Test

Table. 2 Kwiatkowski-Phillips-Schmidt-Shin (KPSS) test.

Time Series	**p-value (Level)**	**p-value (at 2nd difference)**	**Lags used**	**Critical values at 5%**
Solid_Impact	0.01	0.12*	2	0.46
P	0.01	0.28*	2	0.46
perCGDI	0.02	0.14*	2	0.46
NCCA	0.01	0.22*	2	0.46
ECCESS	0.01	0.10*	2	0.46
ATFP	0.02	0.10*	2	0.46

Source: Authors' computation (2024) using tseries package on R version 4.4.0 (2024-04-24 ucrt)

The asterisk * denotes the acceptance of Null that the series were stationary at 2nd difference

The above result shows that all the series have p-values below 0.05 for all the series, the results indicate non-stationarity at the level. However, upon performing the second differencing, we see that the p-values increase, leading to a conclusion of accepting the null hypothesis of stationarity for the second difference (Kwiatkowski et. al., 1992).

2.2 Cointegration Analysis

Table. 3 Johansen Cointegration (Source: Authors' computation (2024) using urca package on R version 4.4.0 (2024-04-24 ucrt)

Test type	**Trace result (with linear trend)**	**Critical Value** (10%)	**Critical Value** (5%)	**Critical Value** (1%)
r ≤3	22.51*	18.90	21.07	25.75
r ≤2	49.27*	24.78	27.14	32.14
r ≤1	513*	30.84	33.32	38.78
r = 0	-	36.25	39.43	44.59

* denotes the rejection of Null, that there is no cointegration relationship

Since the test statistic is greater than all the critical values given at 10%, 5%, and 1% and statistic 22.51 at 10% and 5%, the research rejected the Null hypothesis H0 of no cointegration. This means there is more than one cointegration relationship between variables and solid biofuel use.

2.3 Model Estimation

Table. 4 Coefficients

Variable	**OLS**	**PLS**	**O-PLS**	**VIP (OPLS)**
Intercept	4246493	-	-	-
In P	-38.26	-4.941e-06	-0.233	0.7812
In perCGDI	5092.764	-9.382e-07	-0.085	0.2865
In NCCA	5.291	5.008e-06	0.207	0.6957
In NCCA*ECCESS	-0.094	-5.426	-0.156	1.8837
In ATFP	-113081	-3.047e-06	-0.561	0.5246

Source: Authors' computation (2024) using stats, plsr(), ropls, caret, dplyr package on R version 4.4.0 (2024-04-24 ucrt). The result of OPLS was achieved by tuning hyperparameter predI:1 and Orthogonal component orth:2.

The differences in coefficient magnitudes across these models reflect how each approach handles data relationships. OLS provides clear and interpretable estimates, essential for understanding individual variable impacts.

In contrast, PLS and O-PLS are more suitable when multicollinearity, overfitting, and underfitting pose a challenge, as they both yield coefficients that emphasize the variance captured by the predictors rather than just their contributions. In OLS the estimated coefficient for the intercept stands at 4246493, signifying a baseline of the response variable when all predictors are zero. This model displays some strong coefficients for the predictors suggesting substantial on the response variable. The PLS model adopts a different approach by addressing multicollinearity, which can obscure the effects of individual predictors in the presence of intercorrelated variables in the case of OLS. This technique significantly downscales the coefficients. For P, the coefficient drops to -4.941e-06, indicating a much-reduced effect compared to OLS, this suggests that PLS captures the variance in the data more conservatively. Similarly for the remaining coefficients.

In the O-PLS model takes further operation by separating the systematic variation associated with the predictors from that related to the response variable. These changes suggest that O-PLS has effectively filtered out noise, focusing more on meaningful predictors only.

The positive coefficient for NCCA at 0.207 demonstrates that the variable still retains its significance in the model, although with a reduced effect size compared to the OLS estimates. The interaction term NCCA * ECCESS shows a negative coefficient of -0.156, again indicating a notable decrease in influence compared to the OLS model. This drastic change emphasizes how O-PLS prioritizes relationships that meaningfully contribute to predicting the response variable over mere correlation through tuning hyperparameters (Lee and Kang, 2020).

2.4 Predictive Accuracy and Generalizability

The table below compares the predictive accuracy and generalizability of three models used in the study: Ordinary Least Squares (OLS), Partial Least Squares (PLS), and Orthogonal Partial Least Squares (O-PLS) with hyperparameter tuning. They are discussed below.

Table. 5 Performance metrics (Source: Authors' computation (2024**)** using metrics package on R version 4.4.0 (2024-04-24 ucrt)

Performance	**OLS**	**PLS**	**O-PLS**
R2	0.3708	0.1304	0.62
Adjusted R2	0.1288	-	-
R2X	-	NA	0.596
R2Y	-	NA	0.928
Q2 CUM	-	-11.20685	0.687
Cross-Validated	0.0085	-	-
RMSE	3015434	5202668	1170000
Residual SE	3,645,000	-	-

OLS: In the OLS model only 37.08% of the variance in the response variable based on the predictors was explained as indicated by the R2. This shows a moderate level of variance explanation (Gelman et al., 2018) which suggests that the model is not capturing all relevant information. The lower Adj.R2 value which accounts for the number of predictors and adjusts for overfitting indicates that the predictors in the model were not very useful in explaining the response.

Also, cross-validated R2 (0.0085) is extremely low close to 0, indicating that the OLS model does not generalize well to unseen data. This suggests poor predictive performance when the model is applied to new datasets.

PLS: Here the R2 is much lower than for OLS (0.1304 vs. 0.3708), meaning that the PLS model explains only 13.04% of the variance in the response variable. This suggests that the model has limited explanatory power in this case. Negative values of Q2 indicate poor predictive performance of the training data, leading to poor generalizability of new data and suggesting a potential overfit or not correctly capturing the relationships in the data (Chong & Jun, 2005; Triba et al., 2014). Root mean squared error was also higher 5,202,668, than that of OLS which shows that the PLS model has higher prediction errors than OLS.

O-PLS: PLS tries to reduce dimensionality by capturing the covariance between predictors and the response (Abdi, 2010). However, if the model is not well-tuned (e.g., by selecting the number of latent components), it can lead to poor predictive performance (Bischl et al., 2023).

The negative Q2 and high RMSE from the PLS model indicate that hyperparameters were not optimally set, leading to poor accuracy and generalizability. However, in the O-PLS after careful tuning of the hyperparameter, The PLS shows significant improvement;

O-PLS shows the highest R2 value of 0.62, indicating that it explains 62% of the variance in the response variable, which is a significant improvement over both OLS and PLS. This suggests that O-PLS better captures the relationship between predictors and the response. The R2X and R2Y values indicate that the model explains 59.6% of the variance in the predictor as well as 92.8% of the variance in the response variable. This suggests an extremely good fit as shown in the observation diagnostics (Figure 1), indicating that the model effectively captures the relationship between predictors and the outcome. Cumulative Q2 close to 0.7 indicates that the hyperparameters tuning was optimal and the model has strong predictive power on unseen data, demonstrating good generalizability. The prediction errors were also much lower than both OLS and PLS (as shown in Figure 2). The O-PLS model's ability to remove irrelevant information from the predictors makes it more robust and generalizable.

CONCLUSION

Hyperparameter optimization aims to find the hyperparameters of a given model that return the best performance as measured on a validation set.

The transition from OLS, PLS to O-PLS shows a significant improvement in predictive power and generalizability, highlighting the importance of hyperparameter tuning and model optimization along the way. O-PLS outperforms both OLS and PLS by capturing the most variance, showing strong predictive accuracy and low prediction error by handling irrelevant components effectively, leading to a much better generalizability and fit.

Limitations and suggestions for further research

This study is limited to data sets from 2000-2020 and hyperparameter tuning using grid search only, as such further research can seek to explore other optimization techniques such as random search and Bayesian optimization.

OLS Residual diagnosis

F-stat= 2.524 (on 5 and 13 DF) P-value = 0.08121

RMSE = 3015434

Residual Standard Error = 3,645,000

Shapiro-Wilk normality test data: residuals W = 0.97464, p-value = 0.8639

Durbin Watson Test (Autocorrelation), DW = 2.4042 P-value= 0.855

Breusch Pagan Test (Heteroscedasticity), BP = 2.955 DF=5 P-value = 0.7069

Observation diagnostics

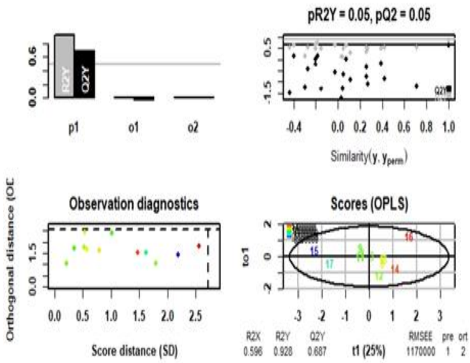

Figure.1 Orthogonal partial least Squares

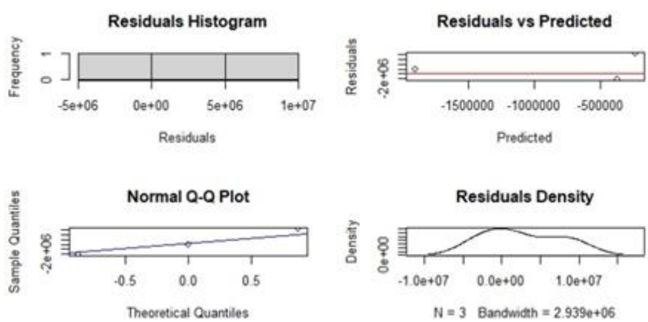

Figure.2 Partial Least Squares

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CHAPTER 4
FOODS WITH A DOUBLE ROLE IN NUTRITION AND HEALTH

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INTRODUCTION

Nutraceuticals and functional foods are largely used to provide medical or health benefits, but there is an urge to determine which products have adequate clinical evidence and a strong safety profile. Nutraceuticals are foods or part of foods that provide medical or health benefits, including the prevention and/or treatment of a disease (1). Functional foods have numerous definitions: they can be defined as processed foods having disease-preventing and/or health-promoting benefits in addition to their nutritive value, but another accepted definition is that they are foods that contain substances, in addition to nutrients, that may have potentially positive effects on health, beyond basic nutrition. These terms often overlap with medical foods, probiotics, designer foods, pharmafoods, and dietary supplements, etc (2).

In light of this evidence, the aim of this study is to explore the scientific and clinical evidence of the positive role of nutraceuticals and functional food in bone health, focusing both on molecular mechanisms and on real-world studies, with the aim of providing a complete list of nutraceuticals and functional foods with adequate clinical evidence usable by everyone to improve bone health and skin (3).

The immune system protects the host against infection from pathological microorganisms and provides constant surveillance for malignant cells that arise over a lifetime. The immune system is able to develop appropriate tolerance to self-proteins, circulating macromolecules, self-cells, and tissues, and to harmless environmental molecules (4)

Nutrients are the substances found in food which drive biological activity, and are essential for the human body. Nutraceuticals may be converted into metabolites by intestinal microbes that serve as biologically active molecules affecting regulatory functions in the host (5).

Individual heterogeneity regarding the intensity of immunological responses exists, largely dependent on genetics, environment, lifestyle, nutrition, and the interaction of these factors. Nutritional immunology is a field of immunology that describes the influence of nutraceuticals on the immune system, antiviral activity, and associated protective functions

Moreover, crosstalk between commensals and the immune system is now recognized because microorganisms can modulate both innate and adaptive immune responses.

The microbiome is vital for immune system development and homeostasis. Gut microbiome and its metabolites might manipulate the local immune responses as well as those of the systemic immune system (6).

Metabolites produced by pathogenic microbes that cross the intestinal barrier trigger pathological conditions, while metabolites produced by saprophytic microbes cross the intestinal barrier and favorable the body.

The immune system plays a vital role in keeping the body healthy by providing a fine balance between the elimination of invading pathogens and the maintenance of tolerance to healthy self-tissue. It is now evident that the gut microbiota has a profound effect on the host immune system and can induce psoriasis (7). The interactions between the gut microbiota and skin are complex, dynamic and context-dependent (8). The gut microbiota and its metabolites have been shown to influence and immune homeostasis both locally and systemically. Antibiotic treatments, vaccinations and hygiene practices all can alter gut microbiota composition (9).

1. Objectıves

The aim of this study is to explore the scientific and clinical evidence of the positive role of nutraceuticals and functional food in skin, and bone health, focusing both on molecular mechanisms and on real-world studies. The objectives were to demonstrate role of nutraceuticals and functional foods in the management of psoriasis, neuropathic pain in dog with spinal cord injury, to demonstrate role of Imuniplant in the management of inflammation in psoriasis and neuropathic pain. The direct modulation of gut microbiome that could diminish inflammatory responses and ameliorate adaptive immune responses.

2. Materials and Methods

This includes the role of macronutrients, micronutrients, and the gut microbiome in mediating immunological effects.

Nutritional modulation of the immune system has applications within the clinical setting, but can also have a role in healthy populations, acting to reduce or delay the onset of inflammation. Ongoing research in this field will ultimately lead to a better understanding of the role of nutraceuticals in inflammation.

Deficiency in macronutrients and/or micronutrients causes impairment of immune function, which usually can be reversed by nutrient repletion.

Figure. 1 Imuniplant tea is a natural immunomodulator of the human microbiome

Imuniplant tea for psoriasis and neuropathic pain in dog with spinal cord injury, it is natural immunomodulator of the human microbiome. Imuniplant tea is a natural genetic immunomodulator of the human and animal microbiome that contributes to the removal of microbiota dysbiosis, can be prevented and removed inflammation. Imuniplant tea contains: cultivated medicinal plants=35%; plant from the spontaneous flora=25%; buds of fruit trees=15%; flowers of fruit trees=15%; berries=10%

Properties: natural genetic immunomodulator, it regulates cellular metabolism, it regulates the central nervous system; it modulates the activity of important neurotransmitters, physically and mentally energizing, remineralizing, it increases resistance to fatigue, natural modulator of the intestinal microbiome. Indicated in: inflammation, autoimmune diseases, metabolic disorders, diseases of the internal organs (liver, kidneys, lungs, hyperacidity), metabolic acidosis, metabolic syndrome, microbiota dysbiosis.

Form of presentation: dry and ground powder packed in tea bags of 1 gram each. 30 envelopes/pack.

Administration: 740 ml of tea that is drunk daily

Duration of treatment: in relation to the evolution of the disease (2-6 months)

Contraindications there are not.

Side effects: they did not appear after long-term use.

Terms of validity: 2 years from the date on the prospectus; it is kept in the dark and at a constant temperature.

Other specifications: it can be used in parallel with the allopathic medication established by the attending physician (10).

With the help of Deniplant brand, Gheorghe Giurgiu has developed several nutraceuticals for psoriasis that act as immunomodulators of the human microbiome. Hence, it is crucial to understand nutraceuticals impact on the psoriatic skin microbiota which is thought to be perturbed, our study provides insight into the skin microbiota in psoriasis and how it is modulated by nutraceuticals and diet.

Figure. 2 Patient with psoriasis

Before treatment After treatment

Because Deniplant treatment addresses the internal causes that trigger and maintain the disease, without ointments or other medications, its duration depends on how quickly the body resolves dysbiosis of the intestinal microbiome, and can be between 4-6 months. If the disease is older, the treatment can exceed 12 months.

After all the lesions healed, there were patients who never had psoriasis again, but there were also patients whose disease reappeared after 10-15 years. Unfortunately, the direct link between the skin microbiota and the pathogenesis of psoriasis remains to be clearly established. The treatment of psoriasis, similar to other immune-mediated complex diseases, is limited to improving the symptoms, due to the lack of effective therapy (11).

Gheorghe Giurgiu created the product Polenoplasmin under the license of the Deniplant brand owner Gheorghe Giurgiu. Polenoplasmin acts as a modulator of the gut microbiome in animals. After he healed his dog that was paralyzed with the hind legs, he watched over 50 cases of paralyzed dogs, and the healing rate was over 80%. Negative results were recorded in paralyzed dogs for a long time (4-6) months.

These studies indicate that gut microbiota modulate inflammatory response. Polenoplasmin for paralysis in dog. Polenoplasmin is a nutraceutical (food with a dual role of nutrition and health) for nerve regeneration of the neuromotor plaque.

Polenoplasmin for veterinary use being a food, it is not medically certified, but its components have scientifically proven healing qualities. It contains freeze-dried pollen from Deniplant plants, carob seed powder, brewer's yeast.

An interesting case of a puppy from Cyprus, who was hit by a car was broken in his spine and was paralyzed with his back legs.

https://www.deniplant.ro/polenoplasmin_catel.htm

For 4 months the puppy was treated with Polenoplasmin, in addition to the physical recovery treatments and the dog was able to walk again.

The puppy lives and walks alone and today as can be seen in the following video: https://youtu.be/OcQ2NXgZnXs, after 6 years the puppy is healthy and can run freely. https://youtu.be/lwzywDfKsnI; https://youtu.be/Z7fcuVWesMc (12-14)

Neuropolen is a nutraceutical (food with a dual role of nutrition and health) for the regeneration of destroyed nerve cells. The use of the components of Neuropolen in the solution of human medical conditions was made long before the appearance of the product under this name. Neuropolen is a natural neuroregenerator of the nerve cell. Neuropolen contains freeze-dried pollen from Deniplant plants, cocoa bean and carob seed powder, brewer's yeast.

Combining them we managed to obtain a product with a wide spectrum of action without side effects or side effects. The components themselves are foods that we can eat daily. That's why Neuropolen has the slogan "Eat and heal" (15).

3. Results

Nutraceuticals and functional foods are largely used to provide medical or health benefits. This review reports the scientific and clinical evidence for the positive role of nutraceuticals and functional food in bone health and gut microbiota, focusing both on in vitro molecular mechanisms, and in vivo animal studies and trials, in order to provide the beneficial effects of some nutraceuticals and functional foods with adequate clinical and experimental evidence useful to improve bone health in real life.

All the described nutraceuticals and functional foods modulated bone cell activity by decreasing osteoclast differentiation and increasing osteoblastogenesis, mainly affecting the oxidative stress and apoptotic signals. The beneficial effects are also evident in human studies. Bone health is the result of a tightly regulated balance between bone modeling and bone remodeling, and alterations of these processes have been observed in several diseases both in adult, pediatric populations, and animals.

Imuniplant modulation of the immune system has applications within the clinical setting, but can also have a role in the aging population, acting to reduce or delay the onset of chronic inflammation. Ongoing research in this field will ultimately lead to a better understanding of the role of nutraceuticals and Imuniplant in chronic inflammation. A dysfunctional immune system can cause a whole range of pro-inflammatory conditions like impaired gut function, weakened responses to new infection.

Imuniplant may restore the composition of the gut microbiome and introduce beneficial functions to gut microbial communities, resulting in amelioration or prevention of gut inflammation and other systemic diseases, like psoriasis.

Evidence for dysbiosis as a source of disease pathology is well-documented in inflammatory skin conditions, such as psoriasis.

An increasing body of literature suggests a crucial role for the gut microbiome in modulating systemic inflammatory disease.

Psoriasis is a chronic systemic inflammatory disease and its pathogenesis is related to the interaction between genetic susceptibility, immune response and environmental triggers, such as diet, stress-level, skin-care routine, etc.

Nutrition plays an important role in the development of psoriasis and it can modulate microbiota and microbiome composition. Correct food choices may have a crucial role in the pathogenesis of psoriasis. Life-style and dietary habits might be related to the incidence and severity of psoriasis.

The treatment of psoriatic patients requires multidisciplinary treatment approach not only at improving skin symptoms, but also at managing metabolic, nutritional, socio-psychological comorbidities that often are associated with this disease.

The gut-skin axis is the novel concept of the interaction between skin diseases and microbiome through inflammatory mediators, metabolites and the intestinal barrier. The dysregulated skin microbiota may become a novel therapeutic target in psoriatic patients.

Psoriasis is a common skin disease, with chronic inflammation and a complex etiology.

The association between the gut and skin is strong and bidirectional, and gastrointestinal health is associated with skin homeostasis. Increasing evidence shows the existence of the gut-skin axis, and that an imbalanced gut microbiome can induce inflammatory skin diseases. The gut microbiome can mediate crosstalk between the immune system and the nervous system by secreting neurotransmitters in psoriasis.

The ”skin-gut axis” concept provides a new insight to investigate the association between the intestinal microbiota and the skin. This offers a feasible approach for improving skin conditions, by the modulation of the gut microbiota. Several types of neurotransmitters secreted by gut microbes were selected to investigate their potential function in psoriasis. Microbiome-mediated interventions could be designed to manipulate these targets for the treatment of psoriasis.

Furthermore, studies also found that an important connection between emotional states and inflammatory skin conditions can be regulated by bacteria of the gastrointestinal tract. Through an extensive review of the literature, we aim to discuss the skin and gut microbiota and redefine their role in the pathogenesis of psoriasis.

Deniplant tea prevents and treats the internal causes that trigger and maintain psoriasis by naturally modulating the intestinal and skin microbiome. Removing dysbiosis from the intestinal microbiota can prevent and eliminate complications caused by psoriasis. It contains cultivated medicinal plants, berries and flora, fruit tree buds. With the understanding that the brain-gut-skin axis exists, it is now clear that intestinal microbes have significant effects on psoriasis.

These results are supported by clinical observations based on a case series showing improvement in psoriatic skin lesions after antibiotic treatment, modulation of gut microbiota by probiotics or fecal microbial transplantation.

We confirmed the association of psoriasis and gut microbiota dysbiosis. This study provides a detailed and comprehensive systematic review regarding gut microbiome in patients with psoriasis. It is still not clear whether psoriasis is an effect or a cause of the observed disbalance between beneficial and pathogenic microbes (11).

The results of this study would be of interest since to our knowledge, microbiome-associated studies targeting spinal cord injury dogs are non-existent and the results might help explain possible implications of gut microbiome in spinal cord injury. We found that gut microbes that metabolize tryptophan - an essential amino acid - secrete small molecules called indoles, which stimulate the development of new brain cells. We demonstrated that the indole-mediated signals elicit key regulatory factors known to be important for the formation of new adult neurons in the hippocampus. This finding is exciting because it provides a mechanistic explanation of how gut-brain communication is translated into brain cell renewal, through gut microbe produced molecules stimulating the formation of new nerve cells (12)

Much less is known about the potential relationship between the composition of gut microbiome and the severity of psoriasis.

These results are supported by clinical observations based on a case series showing improvement in psoriatic skin lesions after modulation of gut microbiota by Deniplant nutraceuticals. Food choices can affect microbiome composition and improve the severity grade of psoriatic disease. There is a strong link between stroke and chronic inflammation. Due to the important link between diet and the gut microbiota, as well as diet and stroke recovery, the gut microbiota may be a potential therapeutic target to safeguard brain function after stroke injury.

The gut microbiota has been demonstrated to influence various brain functions along the “gut-brain axis”. When blood flow to the brain is stopped or reduced during a stroke, some brain cells die because they stop getting the oxygen and nutrients they need.

Due to its composition rich in antioxidants, anti-inflammatory agents, amino acids, minerals and natural vitamins, neuroregenerative molecules, the product Neuropolen offers various possibilities to balance the processes that take place in the nerve cell. Being a food, it is not medically certified, but its components have scientifically proven healing qualities.

The gut microbiota is closely associated with the pathophysiology and prognosis of stroke. Ischemic stroke alters the gut microbiota composition, but conversely, the gut microbiota can also increase the risk of a stroke occurring and play a role in stroke pathogenesis.

Stroke is the most common cause of adult disability. Stroke may begin in the gut, and is closely related to the imbalance of gut microbiota. Modification of the gut microbiota composition by nutraceuticals may create new preventive and therapeutic options in stroke. Existing evidence suggests that nutraceuticals and lifestyle changes may reduce disability and save lives.

This study is another intriguing piece of the puzzle highlighting the importance of lifestyle factors and diet.

An immune response is a reaction which occurs within an organism for the purpose of defending against foreign invaders.

There are two distinct aspects of the immune response, the innate and the adaptive, which work together to protect against pathogens. Alterations in the gut microbiome affect the immune system balance via the production of metabolites.

Microbes coexist with humans and play an important role in regulating health and disease. Immune dysregulation is any proposed or confirmed breakdown or maladaptive change in molecular control of immune system processes (12).

Memory T and memory B cells are also produced in the case that the same pathogen enters the organism again. The innate immune response is an organism's first response to foreign invaders. The innate immune system consists of physical barriers such as skin and mucous membranes, various cell types like neutrophils, macrophages, and monocytes, and soluble factors including cytokines and complement. For example, dysregulation is a component in the pathogenesis of psoriasis. The microbiome is vital for immune system development and homeostasis. Immune deficiencies may be temporary or permanent (13).

Temporary immune deficiency can be caused by a variety of sources that weaken the immune system. Pregnancy also suppresses the maternal immune system, increasing susceptibility to infections by common microbes. Probiotics may restore the composition of the gut microbiome and introduce beneficial functions to gut microbial communities, resulting in amelioration or prevention of gut inflammation and other intestinal or systemic disease phenotypes (14).

A well-functioning immune system is critical for survival. The immune system must be constantly alert, monitoring for signs of invasion or danger. Cells of the immune system must be able to distinguish self from non-self and furthermore discriminate between non-self molecules which are harmful (e.g., those from pathogens) and innocuous non-self molecules (e.g., from food) (15).

CONCLUSION

This presentation describes how nutraceuticals, and functional foods, and intestinal luminal conversion by gut microbes play a role in chronic inflammation. The gut microbiota is considered to be a master regulator of inflammatory homeostasis. Besides modifying the gut microbiota, Imuniplant modulates the immune system in psoriasis, neuropathic pain in dog with spinal cord injury. Probiotics have been widely reported to act on the inflammation.

They are living microorganisms with immunomodulatory effects that stimulate Th1 cytokines and suppress the Th2 response, which are being researched for the treatment of several inflammatory diseases. Probiotics most commonly used are part of the intestinal microbiota like lactobacilli, bifidobacteria, and enterococci.

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