

Fertilization, Eco-Friendly Pest Control, and Their Impact on Clinical Outcomes

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Abstract

Vertical Farming has become essential in sustaining food security, particularly in high-density populated urban environments. In this study, we evaluated an integrated management approach utilizing intelligent nutrient provision and environmentally friendly pest control in controlled environment agriculture. We applied a circular fertilization program by combining a recycled phosphorus source made from struvite with rhizobium bacteria for indigenous nitrogen fixation. In trials with *Phaseolus vulgaris*, an 18% increase in plant growth and 22% and 27% reductions, respectively, in nitrate and phosphate runoff were obtained compared to standard fertilization. For the control of pests, we used a preventive Integrated Pest Management. Finally, adjusting Zinc and Calcium levels, we activated the plants' innate immune systems, which reduced infection from this disease by 35%. Beneficial microbes like *Trichoderma* and *Bacillus* were also introduced to strengthen this natural defense. These combined significantly reduced the effect of chemical pesticides. Overall, our studies suggest that VF can be highly productive and environmentally sustainable. Using nutrients, plant protection, and supporting microbial allies provides a realistic, scalable path toward urban farming systems that are free from chemical residues.

Keywords: Vertical Farming; Integrated Pest Management; Eco-Friendly Pest Management

Introduction

Food security is severely hampered by feeding the world's expanding population, which is expected to reach almost 10 billion people by 2050, particularly in light of resource limitations, water scarcity, land degradation, and climate change^{1,2}. Extreme weather, soil erosion, and inefficient water use are all having an increasing impact on traditional agricultural systems, undermining both environmental sustainability and productivity³. Vertical farming, which uses soilless systems like hydroponics and aeroponics to produce crops year-round in controlled environments, has become a promising approach that reduces reliance on the climate, diminishing land footprint, and conserves water^{1,4,5}.

However, vertical farming also gives its own set of challenges. One of the main issues is the high energy consumption required for lighting, climate control (heating, cooling, ventilation), and maintaining optimal growth conditions. For instance, specific energy consumption for lettuce production in vertical farms is around 10–18 kWh per kilogram under current facility designs, and energy use per cultivated area can range from ~400 to 1,260 kWh m⁻² per year depending on technology and location^{5,6}. If these high energy requirements are not reduced through effective system design, integration of renewable energy, and optimized operations, the environmental benefits may be outweighed⁷.

In addition to energy and resource use, sustainable fertilization practices are critical in vertical farming. Because many vertical farms use nutrient solutions directly (rather than soil), there is a risk of nutrient waste, runoff, or environmental pollution. Studies have shown that replacing conventional field-grown produce with vertical farm produce.

Production in certain regions can reduce nitrogen and phosphorus footprints by around 36-37%⁸. Sustainable fertilization increasingly requires techniques like water quality monitoring, organic or biofertilizers, precise nutrient delivery matched to plant needs, and nutrient recycling^{5,9}.

Another key dimension is pest and disease management. Although controlled environment agriculture reduces some pest pressures, dense planting, high humidity, and limited natural predator populations can promote outbreaks of pests and pathogens. Eco-friendly pest management approaches including Integrated Pest Management (IPM), biological control agents, use of disease-resistant cultivars, sanitation protocols, physical barriers, and monitoring systems are essential to ensure food safety, minimize chemical usage, and maintain ecological balance^{8,10}.

Therefore, while vertical farming has strong potential to improve food security, land and water use efficiency, and year-round production, its sustainability hinges on adopting advanced fertilization strategies and eco-friendly pest management. Without them, trade-offs in energy usage, nutrient pollution, and chemical dependency may compromise the long-term viability of vertical farms. This paper examines recent developments in sustainable fertilization and pest management in vertical farming, identifies gaps, and suggests pathways toward more resilient and environmentally benign systems.

Vertical farming concepts and systems

Vertical farming gained a new meaning when geologist Gilbert Ellis Bailey coined the term in his book in 1915 to enhance root development and suggested deep tilling of the earth. Vertical farming allows us to imagine future food security. Vertical farming, the practice of cultivating crops in layers that are stacked vertically, is essential. It has many advantages, such as increased nutrient and water efficiency, reduced use of pesticides and herbicides, and less agricultural pollution. With a yield that might be 70–80 times greater than that of traditional farming, it offers a way to increase food production¹¹. Perceived sustainability influences consumer acceptability of vertical farming methods; larger systems are generally viewed as more sustainable. Vertical farming is heavily reliant on technology-driven systems like the internet of things (IoT) in the future, although climate control. The use of vertical farming varies depending on size, density, building type, location, level of control¹².

Hydroponics

Vertical farming employs the hydroponics technique, which grows plants in nutrient-enriched liquids without the need for soil. To maintain the right chemical balance, plant roots are submerged in a nutrient solution that is continuously monitored¹³.

Aeroponics

The term “aeroponics” was introduced by NASA in the 1990s to describe the growth of plants in space without soil or large amount of water. But, it still considered unconventional, aeroponic systems are increasingly prevalent in vertical farming. These systems use up to 90% less than hydroponic systems¹⁴. These methods are used in seasonal plant cultivation, commercial production, and research.

Substrate-based Systems

These non-soil mediums are widely used in vertical farming because they can retain moisture, provide a stable environment for plant roots, and can be based on specific systems and crops needed to grow. Some common types of growing media in vertical farming include:

Peat

Peat is an excellent method for supporting plant growth due to its chemical, physical, and biological properties for plant growth. These characteristics may vary depending on the conditions in which the peat is produced. For example, compared to older and more decomposed deposits, younger and less decomposed peats can have different characteristics and have a better water-holding capacity. Manufacturers of plant-growing media are moving toward a future with less peat owing to rising consumer knowledge of environmental issues¹².

Rockwool

Rockwool, also known as stone wool, is an insulation material made by melting natural basalt rock and recycled slag at very high temperatures. Rock wool can be mixed into the soil or used as a chopped substrate component. Rockwool is commonly used media in vertical farming due to its various properties. It provides water retention capabilities, allowing for efficient nutrient uptake by plants. Additionally, rock wool provides good air circulation around the roots¹².

Coco coir: a sustainable growing medium

Coir is a natural fibre derived from the husks of coconuts and has a variety of uses ¹⁵. Its physical characteristics, such as its capacity to retain water and allow proper aeration, before being used as a growth medium, coir needs to be washed many times in fresh water and undergo a "buffering" procedure, which involves adding calcium nitrate to the material for the replacement of dangerously high amounts of salt and potassium. It is eco-friendly, renewable, and biodegradable. Vertical farming uses coir to grow a variety of crops. As shown in Figure 1 and corroborated by the data presented in Table 1, the comparison between vertical farming and conventional agriculture reveals distinct differences in space requirements, water usage, and reliance on pesticides and fertilizers.

Table 1. Comparison with conventional agriculture

This table outlines the difference between vertical farming and traditional farming (location and space, water consumption, the use of pesticides and fertilizers, and growing medium)

	Vertical Farming	Traditional farming
Location and Space	Depends on building rooftops, stacking crops vertically to increase output	Depends on vast areas of land
Water Consumption	It uses significantly less water; hydroponics uses 70% less water, while aeroponics uses 70-90% less water than hydroponics.	It consumes large quantities of groundwater for irrigation
Use of pesticide and fertilizers	It can eliminate the need for these chemicals because of its controlled conditions	It requires large amounts of pesticides and fertilizers
Growing Medium	It is a soilless method	It uses soil

Role of Fertilization in Vertical Farming

Macronutrients and Micronutrients Requirements.

A vertical farm is built around six essential structural components that together create ideal conditions for growing crops in multiple layers (Figure 2). One of the key components is the hydroponic system, which supplies plants with essential mineral nutrients such as nitrogen (N), phosphorus (P), potassium (K), calcium (Ca), magnesium (Mg), sulfur (S), iron (Fe), manganese (Mn), zinc (Zn), boron (B), copper (Cu), molybdenum (Mo), and silicon (Si) directly to their roots. This can be achieved through various methods: a stagnant aerated solution (deep water culture), a thin flowing layer of nutrient solution (nutrient film technique), alternating water levels (ebb and flow), nutrient misting (aeroponics), or drip irrigation to individual plants.

Plants are supported by either inorganic media (like mineral wool, perlite, or sand) or organic media (such as peat, coir pith, or wood fiber), which provide stability for roots, maintain a balanced water-air environment, and act as buffers for pH and nutrients. This controlled rooting environment is particularly important during seed germination and early plant development.

Nutrient Solution Management and Precision Control

In a vertical farm, the nutrient solution is continuously recirculated. However, its composition can change over time due to precipitation, complexation reactions, and the plants' selective uptake of nutrients ¹⁷. For instance, differences in nitrogen absorption can alter the $\text{NO}_3^-/\text{NH}_4^+$ ratio, potentially leading to toxicity symptoms ¹⁷. Variations in the availability of iron can cause deficiencies, while slow uptake of sodium (Na^+) can gradually increase its concentration in the solution ^{18,19}. Antagonistic nutrient interactions, such as the effect of NaCl on potassium (K^+) and nitrate (NO_3^-) absorption or ammonium (NH_4^+) inhibiting K^+ uptake, can further complicate nutrient balance ¹⁷. To manage these challenges, EC-based hydroponic systems are commonly used, as they allow nutrient adjustment through stock solutions without relying on expensive and often inaccurate long-term ion sensors ¹⁹.

Recirculating nutrient solutions can also accumulate phytotoxic organic acids released by roots. To mitigate this, techniques like activated charcoal filtration, electrodegradation, and slow sand filtration are applied, though they may not always be fully effective or cost-efficient, sometimes forcing growers to flush the solution entirely.

Although hydroponic systems generally have lower pathogen loads than soil-based systems, pathogens can still

spread rapidly through the shared nutrient solution. To prevent this, microbial growth is controlled using disinfection methods such as hydrogen peroxide, filtration, heat treatment, ozone, or UV radiation ^{19,20}.

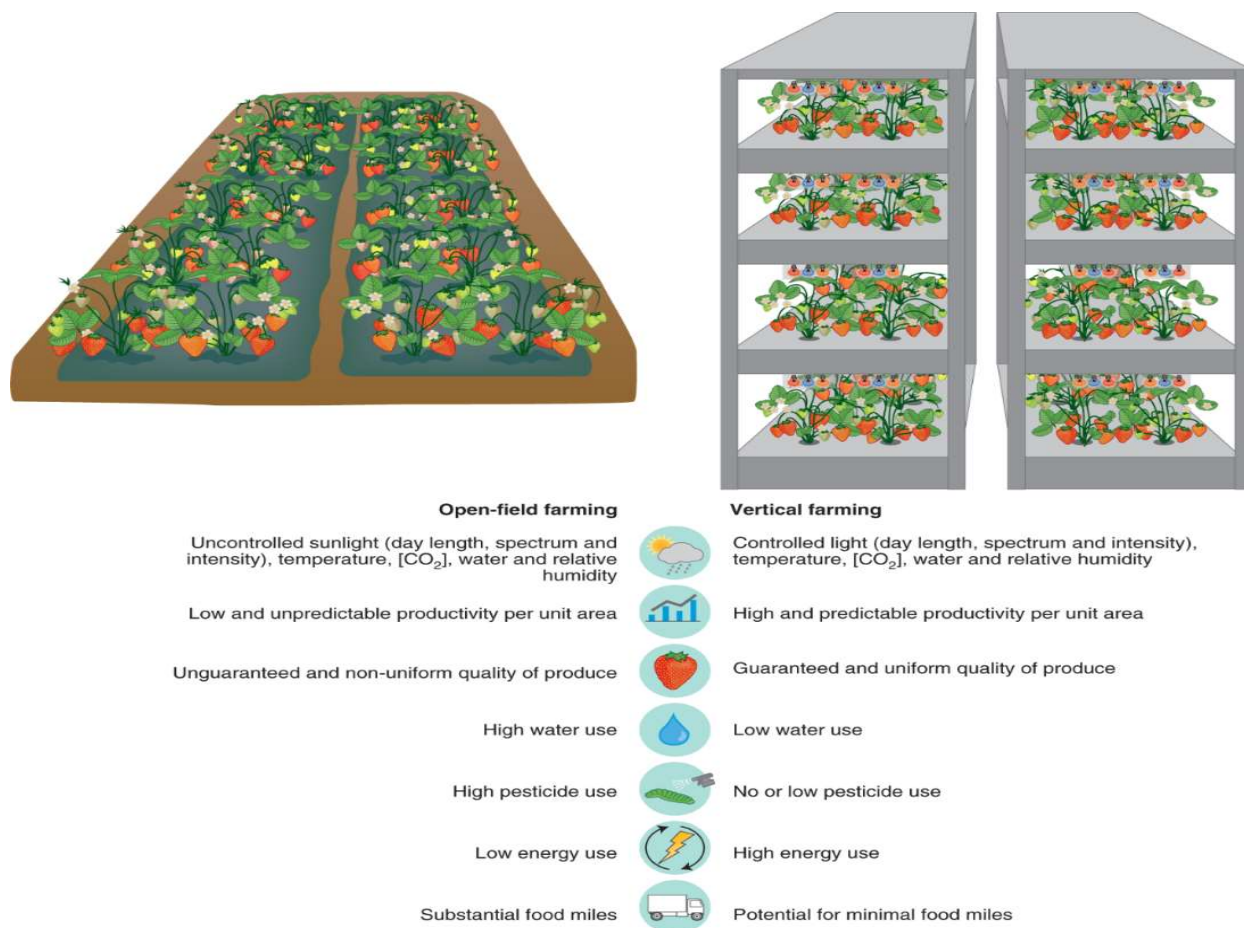


Figure 1. The key comparison between open-field farming and vertical farming is that, by these comparison as we see there are a big difference in temperature, light, water use and energy ^{10,16}.

Biofertilizers and Microbial Inoculants

In recent years, various strategies have been proposed for implementing organic fertilization in vertical farming, which follows a circular economy approach to minimize the introduction of new resources into urban areas. Examples include fertilization using gray water and urine, as well as biofertilizers like rhizobium for legume cultivation, providing an essential nitrogen source for plants. Other approaches involve the use of sewage sludge, sewage sludge ash, and struvite as alternative sources of phosphorus. While these methods can reduce reliance on conventional inorganic fertilizers, they often lead to lower crop yields and, in some cases, require additional infrastructure for irrigation systems. Most studies focus on a single nutrient alternative and do not explore combining multiple approaches, leaving room for innovative solutions that supply various minerals without added infrastructure or environmental burdens.

Smart Fertilizers (controlled-release, nano-fertilizers)

Struvite ($\text{MgNH}_4\text{PO}_4 \cdot 6\text{H}_2\text{O}$) is a crystalline byproduct of wastewater treatment that forms through natural or induced precipitation, usually containing high levels of nitrogen and phosphorus ²¹. It is regarded as a promising slow-release fertilizer due to its nutrient composition, averaging 12.5% phosphorus, 9.9% magnesium, and 5.7% nitrogen, which supports healthy crop development ^{22,23}. Due to these properties, research has focused on optimizing struvite production from wastewater to provide a sustainable alternative to depleting phosphate rock resources ^{22,24}.

Another advantage of struvite is its slow solubility in granular form under neutral to alkaline soil conditions ²⁴, which reduces the risks of nutrient leaching and water eutrophication compared to highly soluble conventional fertilizers ²³.

Additionally, removing 30–40% of nitrogen and phosphorus from wastewater to produce struvite can help prevent eutrophication in urban water systems. The granular form also makes struvite easy to handle and apply, whether mixed into soil or used in hydroponic systems. Its use in agriculture has shown promising results with minimal or no reduction in crop yields ^{22,23}.

Although struvite contains nitrogen, leguminous crops typically require higher nitrogen levels. Therefore, additional nitrogen is often needed, which can be supplied through *Rhizobium* bacteria. These bacteria form a symbiotic relationship with legumes, creating root nodules that fix atmospheric nitrogen into ammonia. The plants benefit from this nitrogen, while the bacteria gain energy from plant-derived compounds. Successful nodulation, however, requires adequate phosphorus and can be influenced by soil conditions, salinity, drought, and initial nitrogen levels.

Using *rhizobium* as a nitrogen source reduces the overall input required for plant growth. In hydroponic systems, initial nitrogen fertilization is sometimes necessary to establish nodulation, after which the bacteria can sustain nitrogen supply for the plants ²⁵. While some studies report slightly lower yields for nitrogen-fixing plants compared to those receiving conventional nitrogen fertilization ²⁵, combining struvite and *rhizobium* can help overcome this limitation ^{26,27}.

To evaluate the effectiveness of these two alternative fertilizers, the ¹⁵N natural abundance method is used to trace nitrogen sources in plants. Plants relying on atmospheric nitrogen fixation show a lower ¹⁵N signature, while plants using other nitrogen sources display higher ¹⁵N levels depending on the fertilizer applied.

This study contributes to the growing knowledge of vertical urban agriculture by exploring the combined use of struvite and *Rhizobium*. The goal is to reduce environmental nitrogen and phosphorus emissions, optimize crop yields, and avoid the need for additional infrastructure. The research focused on the growth, development, and production of common bean (*Phaseolus vulgaris*) fertilized with this combination, demonstrating a cost-effective, space-efficient approach that promotes nutrient recycling within cities. A conceptual layout of the vertical farm system used in this study is shown in Figure 2.

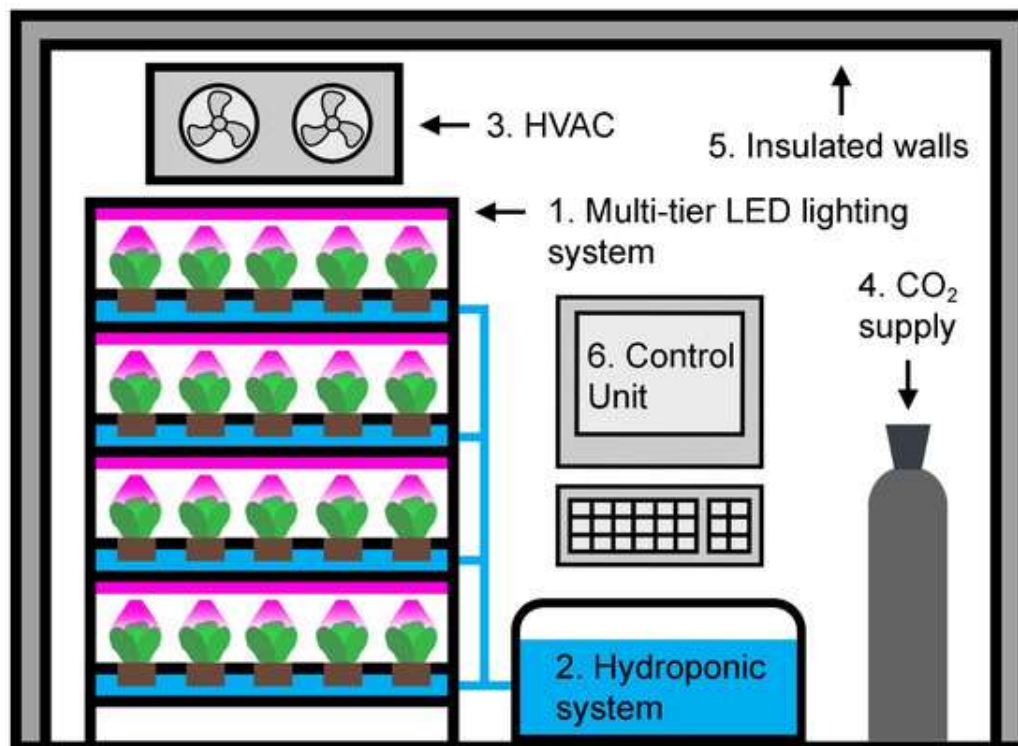


Figure 2. The layout of a vertical farm

(1) A multi-tier system with light-emitting diode (LED) lighting elements; (2) a hydroponic system; (3) a heating, ventilation, and air conditioning (HVAC) unit; (4) CO₂ fertilization; (5) thermally well-insulated and airtight walls; and (6) an environmental (i.e., light, temperature, humidity, CO₂, and airflow) and nutrient solution (i.e., electrical conductivity (EC), pH, O₂, root zone temperature) control unit ²⁰

Pest and Disease Challenges in Vertical Farming

Vertical farming, as a new, quickly developing branch of agriculture based on formerly non-traditional methods of production, presents novel challenges in the control of disease and pests. Normal methods must be radically revised or rethought because of the usual environmental parameters and methods of production for vertical farming. This study discusses the implications of vertical farming conditions on the occurrence of diseases and pests, specifically from herbivorous organisms and vector-borne plant diseases ²⁸. A comprehensive mindmap illustrating the interconnected challenges of pests and diseases and the strategies for integrated pest management (IPM) in vertical farming is presented in Figure 3.



Figure 3. The challenges of pest management and diseases

This mindmap illustrates the interconnected challenges of pests and diseases in vertical farming and the comprehensive strategies employed in Integrated Pest Management (IPM) to address them. It highlights the various types of threats and the multifaceted approach required for effective control

Sources of Pest and Pathogen Entry

Microbial contamination in controlled environment agriculture (CEA) systems can originate from multiple routes of ingress, including the irrigation water, the plant growth substrate, plant nutrition solutions, ventilated air, and inadvertent introduction by personnel ²⁹.

The nexus of water and substrate

While irrigation water is typically treated to reduce its inherent microbial load, the common practice in CEA systems of recovering and recycling this water throughout the different compartments can lead to microbial enrichment. Consequently, a continuous filtering and sanitation step is essential before water reuse. In contrast, plant growth substrates are generally considered single-use media and represent another potential entry point for microbes. However, substrates significantly contribute to the microbial communities recruited to the plant rhizosphere. These microbes are subsequently washed out and collected with the used water, establishing a direct, reciprocal relationship between these two distinct CEA-associated environments.

Principal pathogens and water as the primary vector

The primary foodborne pathogens of concern include Shigatoxigenic *Escherichia coli*, *Salmonella enterica*, and *Listeria monocytogenes*. For these, contaminated irrigation water is widely recognized as the principal source of outbreaks. Although CEA facilities typically mitigate risks associated with traditional horticulture, such as avoiding surface water irrigation and minimizing human contact via automated irrigation water remains a common denominator for both field-grown and protected edibles. This is evidenced by the first reported US outbreak of *S. enterica* serovar Typhimurium linked to CEA, which was attributed to contaminated irrigation water in leafy greens (FDA 2022) ²⁹.

The specific risk of rainwater collection

The collection of rooftop rainwater can introduce an increased level of pathogenic micro-organisms, notably *Cryptosporidium* and *Salmonella* species. This risk is primarily due to contamination from animal droppings, such as bird guano ³⁰.

Common Fungal, Bacterial, and Viral Issues in Vertical Farming

This segment discusses how certain environmental factors inherent in vertical farming humidity, temperature, air movement, and light quality are accountable for the occurrence, persistence, and spread of severe plant diseases caused by fungal, bacterial, and viral pathogens.

Fungal problems

The micro to small size of microorganisms, including fungal spores (e.g., conidia of the downy mildew pathogen of lettuce, *Bremia lactucae*), allows them to penetrate even the most secure 'pest-proof' production systems.

Spores of a number of plant pathogenic fungi, for instance, grey mould (*Botrytis cinerea*), are spread by air movements ³⁰.

Higher humidity offers the best environment for pathogen development (e.g., powdery mildews).

Humidity buildup in the restricted airspace between shelves may be the cause of disease development conditions.

Dropping water between levels. It can be a vector for causing overdevelopment of disease through dispersal of fungal spores ²⁹.

Similarly, fungal spores can fall from higher to lower levels under the mere pull of gravity, likely to facilitate infection spread.

As a natural occurrence, in recirculating hydroponic systems, it is normal for fungi such as *Pythium* to develop and multiply ²⁹.

Best high or low temperatures can reduce host plant resistance to bacterial, viral, fungal, and nematode disease-causing pathogens ²⁸.

Spectral characteristics of LED light control disease progression in viral, fungal, and bacterial causes.

With fungi, light inhibition of sporulation and germ tube formation is highly wavelength-dependent; for example, near UV light provokes and blue light suppresses sporulation in *B. cinerea*.

Red light has also been demonstrated to enhance resistance, for example, to the leaf spot disease *Alternaria tenuissima* on broad bean (*Vicia faba*) ²⁸.

And powdery mildew (*Sphaerotheca fuliginea*) on cucumber (*Cucumis sativus*)³¹.

Bacterial problems

Plant disease can be introduced through a variety of mechanisms.

Droplets of water falling between levels can transmit disease by transferring bacteria.

Sub-optimal temperature has been shown to lower host plant resistance to bacterial, viral, fungal, and nematode disease-producing pathogens³².

LED light spectral content affects virus, fungal, and bacterial disease progression.

Sliding movement in rotation systems can aid in spore dispersal of fungi, insects, and bacteria through mechanical disruption of water droplets and vegetation.

Viral problems

New concerns arise regarding appropriate disease and pest control, causing damage through herbivory and plant pathogen transmission as O-vectors ²⁸.

Less than ideal high or low temperatures can reduce the resistance of plant hosts to bacterial, viral, fungal, and nematode diseases³².

The spectral makeup of LED lighting affects the development of diseases caused by viruses, fungi, and bacteria. Insects like thrips (*Frankliniella occidentalis*) may transmit disease. The perceived effectiveness and relative importance of various proactive pest and disease management strategies, such as biosecurity, sanitation, and monitoring, are visually contrasted in the radar chart shown in Figure 4.

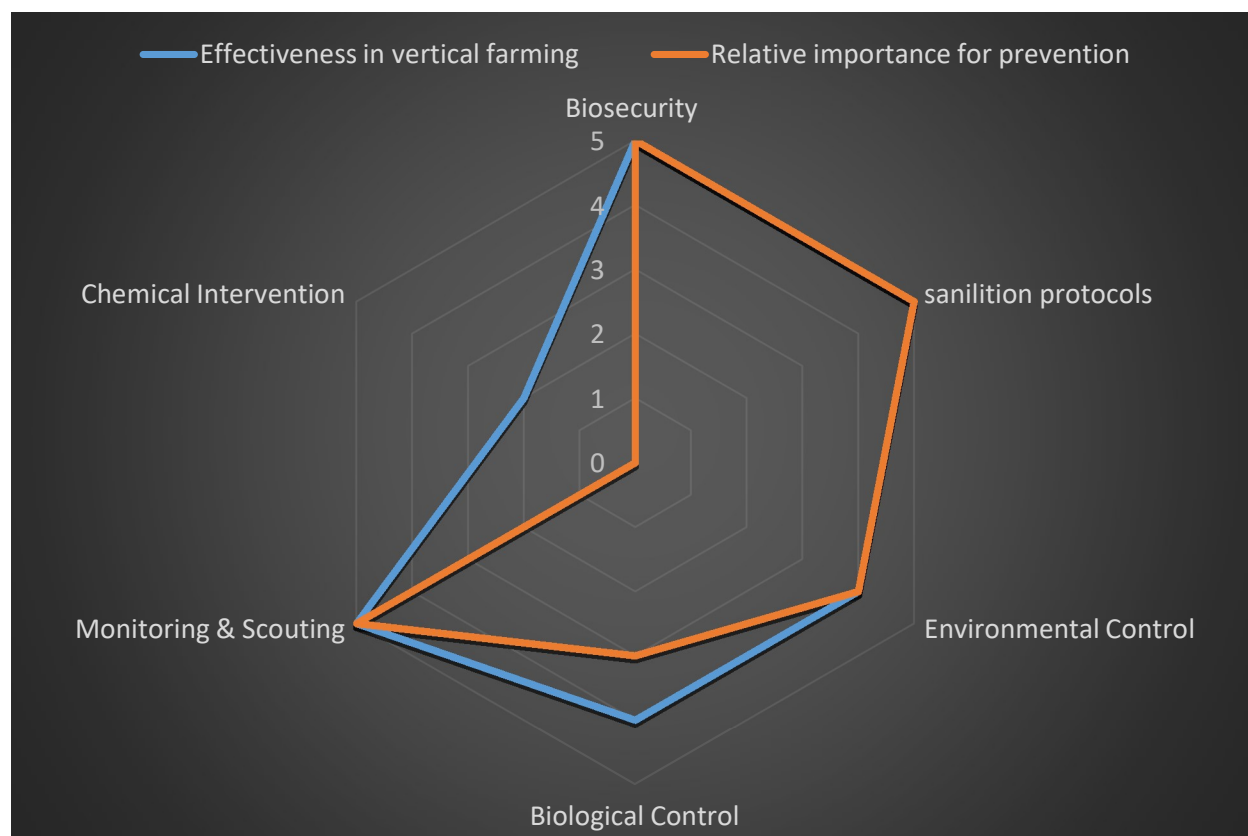


Figure 4. Regular inspections and preventative measures are essential to keep pests at bay in vertical farming operations

The radar chart above illustrates the perceived effectiveness and relative importance of various pest and disease management strategies in vertical farming on a scale of 0 to 5. It highlights that proactive measures like biosecurity, sanitation, and monitoring are highly effective and crucial for prevention, while chemical intervention is considered less effective and less important for prevention in these controlled environments.

Impact of Humidity and Enclosed Environments on Pest and Disease

The study emphasizes the control exercised by protected cultivation (the enclosed environment) and cites humidity as being amongst the factors regulated:

Cropping shields crops against adverse conditions and regulates macro and micro-environments. Control by this increases water use, optimizes plant performance, extends production, enables early ripening, and ultimately optimizes yield and product quality ³³.

If other environmental factors are optimal, light intensity profoundly impacts vegetable nutritional quality, followed by the levels, spectrum of light, temperature, and humidity ³³.

Humidity and disease spreading.

Crop transpiration and evaporation of uncovered hydroponic nutrient solution contribute to humidity rise.

A rise in humidity facilitates conditions for the development of pathogens.

These are pathogens like powdery mildews ³⁴.

A rise in humidity build-up in closed airspace between levels of stacked vertical farming systems can facilitate conditions for disease development.

Proper humidity control is hence important to minimize pests and diseases in closed systems such as vertical farms.

Dispersal mechanisms in closed stacked systems

The increased height of vertical farming growing systems compared to conventional facilities can create significant gradients of temperature, humidity, and light availability from the top to the bottom of the facility.

Whereas air movement is required to provide uniform conditions and help control the majority of diseases, air movement can also assist in the spread of pests and diseases within the crop.

Spores of the majority of plant pathogenic fungi, for example, grey mould (*Botrytis cinerea*), are spread by air

movement³⁵.

Condensation along the undersides of stacked growing levels can form water droplets that could precipitate onto lower-placed plants.

The droplets could enable disease spread by dispersal of fungal spores.

Water droplets falling between levels could be a conduit for enabling disease spread.

Fungal spores or insects may also fall from top to bottom shelves by gravity alone, facilitating infection spread.

Pest and pathogen access

While glasshouses and CE systems reduce pests' and diseases' access, in reality, they cannot be realistically expected to exclude them altogether.

Practically, it is considered impossible to exclude many pests and pathogens from glasshouses.

The likely means of introduction will be through ventilation systems and doors.

Their diminutive size, for example, fungal spores (e.g., the conidia of *Bremia lactucae*), will enable them to pass even through the most well-serviced 'pest-proof' systems.

Advocates of vertical farming and urban agriculture systems contend that their implementation will prevent all insect and disease entry and abolish any pest management requirements due to their placement in secure buildings. Even though glasshouses and particularly CE systems prevent the entry of pests and diseases, they cannot practically be expected to entirely remove the occurrence of pests and diseases in a crop. Indeed, it has been considered virtually impossible to exclude most pests and diseases from glasshouses.

The most likely method of entry is through ventilation systems and doors.

Despite this, the very small size of microorganisms, e.g., fungal spores (e.g., conidia of *Bremia lactucae*, the lettuce downy mildew pathogen), arthropod pests (e.g., two-spotted spider mite (*Tetranychus urticae*)), and insects (e.g., western flower Thrips (*Frankliniella occidentalis*)) permits their entry into even highly maintained pest-proof protected growing systems.

Effects of air circulation and humidity

The higher vertical farming growing systems' height than conventional facilities may imply substantial temperature, humidity, and light access gradients from bottom to top in the facility. While air movement is needed to provide equal temperatures, water content, and levels of carbon dioxide for plant growth and help control most of the diseases, air movement also helps to spread the pests and diseases throughout the crop. Spores of most of the plant-pathological fungi, such as grey mould (*Botrytis cinerea*), have been found to be blown away by air movements.

In protected cultivation systems, transpiration of the crop and hydroponic nutrient solution evaporation in contact with the air result in increased humidity, which is to the advantage of crop development, but allows for favorable conditions for pathogen proliferation (e.g., powdery mildews and *B. cinerea*). Humidity buildup in the restricted airspace between planes in vertically stacked systems can pose conditions for disease development. High humidity also accelerates insect activity, which could result in increased pest damage. Low humidity can potentially foster particular pests, like spider mites. Precise control of humidity is therefore essential to minimizing pests and disease in closed environments such as vertical farms.

Condensation and dispersal

Condensation on the bottom of stacked growing levels can create water droplets that can drip back onto the surface of plants developing on the level below. Such droplets would be capable of causing the spread of disease by dispersing fungal spores or bacteria as has been found from droplets falling from glasshouse roofs or overhead watering. Therefore, water droplets that fall between tiers in vertical farms due to humidity condensation, either from irrigation or growing medium, can be a vehicle for disease spread. Similarly, insects or fungal spores can fall from higher to lower shelves by gravity alone to facilitate the spread of infection or damage from top to bottom shelves, even without water droplet help. These unique challenges related to rapid disease spread and environmental control are contrasted with traditional farming environments in Table 2.

Eco-Friendly Pest Management Strategies

Preventive Measures

The first Line of sustainable defense, preventive measures form the bedrock of any successful sustainable pest management (SPM) system, adhering to the principle that prevention is superior to treatment. These strategies focus on establishing physical and hygienic barriers to deter pest establishment. Key practices include rigorous hygiene protocols for all cultivation facilities and equipment, alongside mandatory seed sanitation to ensure propagation

begins with material free of latent pathogens. Furthermore, in controlled environments, air filtration becomes a crucial process, actively blocking airborne spores and insect pests from entering, thus significantly reducing the necessity for subsequent, more resource-intensive control methods ³⁶.

Table 2. The contrasting environments and challenges faced by traditional and vertical farming in managing pests and diseases

Feature	Traditional farming	Vertical farming
Environment control	Open, highly variable weather-dependent	Closed, highly controlled. (temperature, humidity, light, PH)
Soil-borne diseases	Significant risk (e.g., nematodes, fungal wilts).	Minimized to absent (soil-free systems).
Pest entry	Easy from surrounding environment, natural dispersal.	Through personnel, contaminated inputs, ventilation, doors
Spread rate	Variable, influenced by wind, rain, and natural barriers.	Rapid due to dense planting, air circulation, recirculating water.
Natural Predators	Present, part of the ecosystem balance.	Absent, requiring deliberate introduction of biological controls
Pesticide Use	Common, often broad-spectrum; environmental impact concerns.	Minimized, targeted, regulatory constraints: emphasis on IPM.
Waterborne Pathogens	Less common, usually specific to irrigation methods.	Significant risk in recirculating hydroponic/aeroponic systems.
Pollination	Relies on natural pollinators (insects, wind).	Requires manual pollination or artificial methods.
Hygiene Requirements	Standard agricultural practices.	Strict, near-sterile biosecurity and sanitation protocols.

Technological Tools

Integrating modern monitoring and sterilization, the agricultural sector is undergoing a revolution driven by the integration of advanced technological tools into pest management. Utilizing Sensors combined with artificial intelligence (AI) capabilities enables highly precise, real-time pest monitoring and disease diagnosis. This precise detection allows for the rapid identification of infection hot spots, facilitating targeted, localized intervention rather than area-wide treatments. In parallel, physical techniques like UV treatment (Ultraviolet) and Ozone application are employed to effectively sterilize water, surfaces, and circulating air in closed systems. These methods offer powerful, residue-free alternatives for reducing the pathogen load in the growing environment ³⁷.

Safe Chemical Pesticides

The Last Resort in IPM, within the context of Integrated Pest Management (IPM), the use of chemical pesticides is treated as an essential last resort, invoked only when the pest pressure surpasses the economic threshold and cannot be contained by biological, preventive, or technological strategies. The focus here is on the highly selective application of environmentally safer compounds, prioritizing those with low toxicity to non-target organisms (such as beneficial biocontrol agents) and a short Pre-Harvest Interval. This approach minimizes both environmental harm and human exposure risks, providing a safety net against catastrophic crop loss while upholding the core principles of sustainability ³⁸.

Biological Management Strategies

We use biological control strategies because they help reduce crop loss in a sustainable, safe, and cost-effective way, in harmony with the components of nature. In addition to its environmental benefits, it is a popular winning card in the economic aspect, and major agricultural and industrial companies are now seeking to implement it for its multifaceted advantages. If we follow traditional agricultural systems and use chemical pesticides, which expose the crop to a decrease in a way that does not meet this increase, in addition to being pathogenic, this will lead to famines

and, consequently, wars. But now, with the applications of sustainable agriculture, which include systematic biological control, it has become possible to find a solution to this disaster, such IPM "integrated pest management" ³⁹. Systematic environmental control is a vast science that develops day by day. With development, the means and mechanisms increase, and thus it is difficult to include them under one heading. Therefore, they are divided into several sections, whether for combating insects, plant diseases, or parasites. Systematic biological control is environmentally safe because it depends on the harmony of the components of the environment and is an application of the natural law of survival of the fittest.

Natural Enemies

We use pathogenic organisms to eliminate each other, such as bacteria, fungi, or even, in some cases, viruses, which gives them priority over harmful, pathogenic, and expensive chemicals ⁴⁰.

Types of Biocontrol

There are four types of biological control. First, conservation control, which is environmental management through human intervention, whether in the plant, soil, or pesticide. Second, natural biological control, which occurs in favor of the plant, but in a natural way, without human intervention. Third, Augmentative biological control, which is the release of a large number of natural enemies in a specific season to eliminate another pest, applying the law of survival of the fittest, but with human intervention. Fourth and finally, classical biological control, which involves releasing a specific type of natural enemies at the beginning of cultivation, but in small numbers, so that it grows and adapts itself, and remains in the soil permanently, eliminating other pests when they appear ⁴¹.

Macroorganism in biocontrol

Macroorganisms are one of the four most important categories of biological control because they are no longer used solely for plant protection but also for their role in expanding the global benefits of plants. As evidence of their importance, France has been using them rigorously in its protection protocols for the past twelve years ⁴². High efficiency of macro-organisms is achieved when utilized within a microbial synergy, analogous to vitamins that boost human health. Key examples of effective macro-organisms include the predatory lady beetles (Coccinellidae) and aphid lions (Chrysopidae), which are characterized by high efficiency in pest control. Although the Trichogramma parasitoid is an essential element in biocontrol programs, its maximum efficacy is often not realized except when utilized concurrently with microbial control agents (such as *Bacillus thuringiensis*). In the previous paragraphs, we talked about the importance of replacing chemical pesticides and old agricultural methods with biological control. We also talked about large organisms and the importance of the presence of small organisms with them, and how they complement each other, but the most effective and efficient are the small organisms ⁴³.

Microorganism in biocontrol

Several effective microbial biological control agents (MBCAs) have been utilized in practical biocontrol protocols. Key examples include bacteria from the genera *Bacillus* and *Pseudomonas*; on the other hand, fungi such as *Trichoderma*, *Aspergillus*, and *Penicillium* have demonstrated efficacy in suppressing the common plant pathogen *Fusarium oxysporum* and some viruses such as bacteriophage and mycoviruses ⁴³. A key applied example of microbial efficacy involves the bacterium *Bacillus velezensis* strain GSBZ09, isolated from grapevines. This potent MBCA exhibits broad-spectrum antifungal activity and actively promotes plant growth through metabolites like Indole-3-Acetic Acid (IAA), significantly reducing the severity of Grape White Rot caused by the fungus *Coniella vitis*. We have another very strong example in fungus in biocontrol. Among fungal MBCAs, the genus *Trichoderma* is considered the gold standard, widely used due to its multifaceted action. It colonizes the rhizosphere and protects plants via mycoparasitism (attacking pathogen cell walls), antibiosis, and fierce competition for nutrients. Species like *T. harzianum* and *T. viride* also promote plant growth, making *Trichoderma* a cornerstone of sustainable fungal biocontrol ⁴⁴. Biological control is not limited to living organisms. Viruses also play a major role and are divided into several types: first Entoviruses, viruses that target insects, work as bioinsecticides and have been used since the nineteenth century to control *Lymantria monacha*. Second (bacteriophages): Viruses that target bacteria such as: *Erwinia amylovora* (causative agent of fire blight in apple and pear), *Xanthomonas* and *Pseudomonas* (causative agent of bacterial spot diseases in tomato and pepper). Third, viruses that target fungi (mycoviruses), A clear example of this is the biological control of chestnut late blight, which weakens the pathogenic fungus *Cryphonectria parasitica* ⁴⁵. After discussing: Augmentation – Large: (*Neodryinus*).

Microbial augmentation (Bacillus, Trichoderma, Baculoviruses)

Conservation and habitat biocontrol

Now we will discuss conservation: (increasing floral biodiversity to support parasites and predators). It is an indispensable strategy within Integrated Pest Management (IPM) to ensure sustainable pest control, aiming to protect and enhance local natural enemies. The strategy is based on increasing floral biodiversity, a common ground between small-scale and industrial agriculture. We have become aware of its importance even before it became an essential part of modern agricultural-industrial environmental management plans to produce green consumer products ⁴⁶. Recent research, such as the study conducted on wheat crops, has demonstrated the effectiveness of this technique by achieving tangible quantitative results. Through the establishment of functionally selected floral strips adjacent to wheat fields, targeting wheat aphids, an increase in control efficiency was observed: the floral strips enhanced the activity of both ladybugs (predators) and parasitoid wasps, leading to a significant rise in the rates of parasitism and predation on the aphid populations. Economic Impact: It was found that applying floral strips across 10% to 15% of the field area was sufficient to provide essential biocontrol services, which ultimately led to a significant increase in wheat yield compared to control fields lacking these strips ⁴⁷.

Biocontrol economical effect

Economically, biological control is highly attractive, as it reduces costs in several ways. Firstly, it increases yields. Secondly, it prevents the overuse of pesticides and chemical equipment and reduces the use of fertilizers. This sustainable choice offers its greatest advantage through increased income and an investment in long-term health that is not dependent on immediate timing.

Future of biocontrol

Not only is the economic aspect of biological control attractive, but its future is also promising in several aspects. First, in terms of the endless commercial applications and expansions of plant-enhancing microorganisms and their being a safe, economical, and sustainable environmental alternative. But in the future, we must also re-study microbes and their effects on plants, as mutations are endless.

Challenges in Biological Control

Despite the economic and environmental advantages and bright future of biological control, it faces certain challenges, and this is the case with biological control. The most important of these challenges is the necessity of testing the microbe used on a wide scale to determine its suitability as a biopesticide. If the microbe proves effective, its effect may change with environmental variations. Furthermore, if it proves effective, it requires extensive scientific knowledge and trained hands to handle it ⁴⁸.

Translational Link to Clinical Studies

How cultivation conditions affect the clinical efficacy of plant-derived therapies, and the importance of reproducible plant quality for clinical trial design

Temperature Stress

Temperature strongly affects plant growth, photosynthesis, and production of secondary metabolites (SMs). Warmer temperatures often boost growth, while cold temperatures slow growth and photosynthesis. However, the effect on SMs depends on the species; it's not the same for all plants: *Duboisia myoporoides* showed a slight increase in alkaloids when the temperature rose by 4 °C ⁴⁹. *Salvia miltiorrhiza* produced more tanshinones under higher temperatures ⁵⁰. *Tithonia diversifolia* had increased phenolic compounds at 22 °C, but they decreased when the temperature went higher ⁵¹. In *Camellia japonica*, low temperature influenced genes related to unsaturated fatty acids and jasmonic acid pathways ⁵². In *Silybum marianum*, high temperature reduced silymarin content. *Dendrobium officinale* grown in wild (cooler) conditions had higher polysaccharide, alkaloid, and flavonoid content than when grown in warmer greenhouse conditions ⁵³.

Ozone Stress

Ground-level ozone (O₃) acts as an oxidative stressor. Many medicinal plants respond by increasing antioxidant compounds: *Hypericum perforatum* exposed to 110 ppb ozone for 5 h increased total phenols and flavonoids, e.g., quercetin ⁵⁴. After 24 h ozone exposure, quercetin dropped, but kaempferol increased instead in the same plant ⁵⁴. *Salvia officinalis* exposed 90 days to ~120 ppb ozone had large boosts in phenolic content e.g., Gallic acid doubled, Caffeic acid increased eightfold, Rosmarinic acid increased 122% on day 60 ⁵⁵. *Capsicum baccatum* var. *Pendulum* under chronic ozone had ~50% reduction in capsaicin and dihydrocapsaicin in pericarp; but pericarp carotenoids and phenolics increased (52.8% and 17%, respectively) ⁵⁶. *Melissa officinalis* treated with 200 ppb ozone for 3 h increased

anthocyanins, phenolics, and rosmarinic acid ^{57,58}.

Light Stress

Light intensity and quality (shade vs full sun, light spectrum) greatly influence SM production: In *Mahonia* species, alkaloid yield was highest under 30–50% sunlight (partial shade) rather than 10% or full sun ^{59,60}. *Flourensia cernua* produced more total phenolics under partial shade compared to full sunlight⁶¹. In *Erigeron breviscapus* (scutellarin) and *Centella asiatica* (chlorogenic acid), sun-developed leaves had more SMs than shade-grown leaves ^{62,63}. In vitro for *Hyptis marrubioides*, white and blue lights increased flavonoid (rutin) levels, while red light improved growth, leaf number, and dry weight.

Ultraviolet (UV) Radiation Stress

UV-B exposure often induces production of protective SMs in plants: *Chrysanthemum morifolium* increased flavonoids and phenolic acids under UV-B ⁶⁴. *Coleus forskohlii* leaves under UV-B had increased phenolics and flavonoids ⁶⁵. *Prunella vulgaris* (spica) irradiated with UV-B increased total flavonoids, rosmarinic acid, and caffeic acid best harvest between budding and full-flowering for maximum medicinal value ⁶⁶. *Kalanchoe pinnata* leaves under UV-B + white light showed a higher phenolic profile and greater amount of quercitrin ⁶⁷.

Soil Water Stress (Drought Stress)

Water shortage (drought) often causes plants to change metabolism and sometimes produce more SMs depending on severity: In *Scutellaria baicalensis*, mild drought increased baicalin content; under severe drought, baicalin decreased ⁶⁸. *Glycyrrhiza glabra* under slight/moderate drought increased glycyrrhizin content, but extreme drought lowered it ⁶⁹. *Ocimum tenuiflorum* tolerated severe drought for 30 days, with major transcriptomic adjustments ⁷⁰. In *Mentha piperita* and *Catharanthus roseus*, drought decreased total phenols, flavonoids, and saponins, but increased tannins, terpenoids, and alkaloids ⁷¹. Another study on *Catharanthus roseus* found that drought significantly increased alkaloids and up-regulated related biosynthetic genes ⁷². In *Thymus* species, drought stress strongly affected sugar, amino acid, and energy metabolism ⁷³. *Stellaria dichotoma* var. *lanceolata* showed increased total saponins under moderate water stress, but levels dropped when stress intensified ⁷⁴.

Soil Salinity Stress

Saline soils (high salt) challenge water uptake and nutrient balance, influencing SM production: *Carthamus tinctorius* leaves increased flavonoids under moderate NaCl (50–150 mM)⁷⁵. *Stevia rebaudiana* showed increased diterpene glycosides at low salinity (30 mM), but content dropped at higher salinity (90 mM) ⁷⁶. *Plantago ovata* had higher phenolic content under 25–300 mM NaCl salinity ⁷⁷. *Brassica napus* var. *oleifera*: total phenolics, non-flavonoids, and tannins increased up to moderate salinity; phenolic acids showed no clear trend ⁷⁸. *Salvia macrosiphon* under increasing salinity (up to 6.8 dS m⁻¹) had a sharp decrease (≈2.6-fold) in total phenolics ⁷⁹.

Soil Fertility and Nutrient Stress

Availability and balance of soil nutrients (fertilizers) affect SM biosynthesis: In *Duboisia* species, high nitrogen and calcium (above 1 mM) correlated with lower scopalamine content; potassium (0.05–4 mM) had no effect ⁸⁰. *Lactuca sativa* produced the highest total polyphenols and antioxidant activity when grown without nitrogen fertilization ⁸¹. In *Trigonella foenum-graecum* (Fenugreek), foliar application of irradiated sodium alginate combined with soil phosphorus increased seed yield by 131%, trigonelline content by ~18%, and overall alkaloid yield by ~208% ⁸².

Examples of medicinal plants where growing conditions influenced therapeutic performance

Several medicinal plants clearly show changes in their therapeutic potential depending on environmental conditions, because these stresses directly affect the levels of key secondary metabolites. For example, *Hypericum perforatum* grown under elevated CO₂ showed reduced hypericin content (about 22% decrease), even though the plant biomass increased. Under combined high CO₂ and temperature, hypericin decreased even further, ⁸³. Since hypericin is the main active compound, these changes may weaken the plant's therapeutic effect. In *Glycyrrhiza glabra*, mild and moderate drought increased glycyrrhizin levels, while severe drought caused a reduction ⁶⁹. This means that water availability directly influences the quality of its medicinal compounds. *Stevia rebaudiana* produced higher amounts of steviol glycosides when exposed to elevated CO₂ ⁸⁴, suggesting improved sweetness and potential medicinal value under CO₂ enrichment. *Prunella vulgaris* treated with UV-B radiation showed an increase in total flavonoids, rosmarinic acid, and caffeic acid ⁸⁵, which are responsible for its anti-inflammatory and antioxidant activity. *Salvia officinalis* exposed to ~120 ppb ozone for 90 days showed major increases in phenolic compounds, with gallic acid doubling and caffeic acid increasing eightfold ⁵⁵. These metabolites strongly contribute to its medicinal efficacy.

These examples demonstrate that the same species can produce different levels of active compounds depending on environmental stresses. Therefore, cultivation conditions directly influence the therapeutic performance of medicinal plants by altering their phytochemical profiles.

Clinical Studies for Patients: Relevance and Applications

Introduction: VF as a Paradigm for Pharmaceutical Consistency

The controlled-environment agriculture (CEA) framework offered by vertical farming (VF) represents a transformative paradigm for the reproducible and high-throughput production of medicinal plants. By enabling precise regulation of environmental parameters, VF minimizes the variability seen in open-field farming and ensures consistent yields and standardized phytochemical profiles, an essential requirement for pharmaceutical-grade materials ⁸⁶.

Sustainable Fertilization Strategies for Enhanced Phytochemical Biosynthesis

In the context of producing pharmaceutical grade biomass, nutrient management extends beyond maximizing vegetative growth to the specific goal of optimizing the biosynthesis of targeted secondary metabolites (e.g., alkaloids, flavonoids, terpenoids). Sustainable fertilization strategies in VF are meticulously engineered to minimize resource consumption while simultaneously elevating the therapeutic quality:

Precision Nutrient Delivery and Resource Efficiency

Hydroponic and aeroponic VF systems allow precise, real-time delivery of optimized nutrient solutions while minimizing water use and nutrient waste. The closed-loop nature of these systems not only improves sustainability but also enhances the reproducibility of medicinal compound biosynthesis under controlled environmental conditions ⁸⁷.

Targeted Nutrient Stress and Chemical Elicitation

Empirical evidence suggests that the application of mild nutrient stress (e.g., temporary restriction of nitrogen or phosphorus) or the use of chemical elicitors (e.g., salicylic acid, methyl jasmonate) within the nutrient solution acts as crucial signaling molecule. These interventions can significantly enhance the concentration and profile of specific phytochemicals within the plant tissue. This approach is intrinsically sustainable as it customizes the nutrient regime to meet pharmaceutical demands rather than merely biomass accumulation ⁸⁸.

Eco-Friendly Pest Management Approaches for Pharmaceutical Purity

The inherent biocontainment of VF significantly reduces endemic pest pressure compared to conventional farming. However, when phytopathogens or pests do occur, the preference shifts strictly towards non-chemical and environmentally benign methods to guarantee the final botanical extract is free from synthetic pesticide residues a non-negotiable requirement for regulatory approval of pharmaceutical materials:

Biological and Physical Control Mechanisms

The deployment of biological control agents (BCAs) (e.g., predatory mites, parasitic wasps) forms the cornerstone of eco-friendly pest management in VF. The contained environment ensures high establishment efficiency and sustained efficacy of the BCAs. Additionally, techniques such as UVA/UVB light treatments and precise environmental manipulation (e.g., strict control of humidity and temperature) are highly effective in suppressing pathogen growth and pest reproduction without the need for chemical intervention ⁸⁶.

Utilization of Biopesticides

Utilizing approved microbial or botanical extracts as biopesticides offers a sustainable line of defense when required, maintaining the focus on product safety and residue-free production ⁸⁷.

Impact on Clinical Outcomes and Pharmaceutical Integrity

The strategic integration of sustainable VF practices directly and positively modulates the clinical outcomes associated with the resulting pharmaceutical products:

Standardization and Therapeutic Efficacy

By precisely controlling all environmental parameters (light spectrum, temperature, CO₂) and applying optimized fertilization/elicitation protocols, VF ensures a highly consistent and reproducible phytochemical profile (Standardization). This consistency is essential for maintaining the therapeutic predictability and efficacy of the herbal medicine or derived drug, thereby leading to more reliable and consistent patient outcomes ⁸⁶.

Safety Profile and Purity Assurance

The mandated use of eco-friendly pest control and closed-loop systems eliminates contamination risks from heavy metals, synthetic pesticides, and pathogenic microorganisms. This results in a purer, safer raw material, which is paramount for extracts intended for human consumption or parenteral administration ⁸⁷.

Advanced Case Studies in VF-Driven Drug Production

VF has demonstrated its utility for the commercial-scale production of high-value medicinal plants, enabling the fine-tuning of bioactive compounds for superior clinical application:

Cannabis (Cannabinoids: CBD and THC): VF allows precise spectral manipulation and targeted nutrient delivery to maximize the biosynthesis of specific cannabinoids, ensuring dose-consistency essential for clinical trials and patient safety ⁸⁹.

Ginseng (Ginsenosides) and Hypericum perforatum (Hypericin): The production of high-value ginsenosides and the active antidepressant compound hypericin is maximized under specific nutrient stresses and light cycles achievable only in VF. Manipulating these factors translates directly to a more potent and reliable botanical drug product.

Integration of Fertilization and Pest Management

Nutrient-driven Enhancement of Plant Immunity

Nutrient management is increasingly recognized as a central pillar of plant immunity, particularly in vertical farming where environmental variables are tightly controlled, and adjusting the balance of macronutrients such as nitrogen, phosphorus, and potassium directly impacts disease susceptibility ⁹⁰. Calcium acts as more than a structural element because it functions as a pivotal secondary messenger that translates pathogen perception into downstream defense activation ⁹¹. Cytosolic Ca^{2+} oscillations serve as “signatures” that are decoded by calcium sensors, ultimately inducing transcriptional cascades linked to defense genes such as PR1 and PAL ⁹².

Nitrogen management in particular is a double-edged sword since excessive application promotes lush tissue that is more susceptible to fungal colonization, while balanced supplementation strengthens systemic acquired resistance ⁹³. The adoption of fertigation systems with real-time monitoring of EC and pH in vertical farms allows precise modulation of nutrient-driven immunity, reducing the vulnerability window for pathogen establishment ⁹⁴. Micronutrient correction is equally critical, as zinc supplementation stimulates antioxidant enzyme activities and stabilizes membranes, resulting in enhanced resistance to fungal and bacterial pathogens ⁹⁵. Manganese contributes by activating phenylpropanoid metabolism and lignin biosynthesis, which reinforce cell walls as the first line of defense ⁹⁵.

Copper, although required only in trace amounts, plays a unique role in triggering broad-spectrum antiviral responses when carefully applied within safe concentration ranges. Boron, often overlooked, is essential for pectin cross-linking in the cell wall, and its deficiency compromises tissue integrity, predisposing plants to pathogen ingress ⁹⁶. Recent transcriptomic analyses reveal that balanced nutrient application shapes ROS dynamics, priming plants for more rapid defense activation under pathogen challenge ⁹⁷. In vertical farms, nutrient programming has been directly linked with enzymatic markers of immunity such as peroxidase and catalase activity, which serve as reliable bioindicators of systemic resistance ⁹⁷. Plant nutrition also reshapes rhizospheric microbiomes, introducing another dimension of indirect disease suppression through microbial competition and ISR induction ⁹⁸. Furthermore, nutrient balance enhances the accumulation of phytoalexins, secondary metabolites that act as chemical deterrents against a broad range of pathogens ⁹⁰. Artificial intelligence-driven fertigation control, integrating nutrient and immunity data in real time, is emerging as a powerful decision-support system for pest management ⁹⁸. Altogether, precise nutrient modulation offers a robust, eco-friendly avenue for boosting plant immunity in vertical farming, reducing dependence on chemical pesticides, and aligning production with sustainability goals ⁹⁸.

Role of Calcium, Silicon, and Micronutrients

Calcium plays a dual role in plant immunity as both a structural element and a secondary messenger, where calcium influx upon pathogen recognition triggers downstream signaling cascades that activate systemic defense responses ⁹⁹.

In vertical farming systems, the adjustment of the Ca: K ratio in nutrient solutions significantly reduces blossom-end rot and vascular leakage, contributing to improved resistance against opportunistic pathogens ⁹⁹. Moreover, calcium binding proteins such as calmodulin translate Ca^{2+} signatures into activation of WRKY transcription factors, which regulate defense gene expression ⁹¹. Research has shown that plants deficient in calcium exhibit higher susceptibility to bacterial and fungal invasion due to compromised cell wall integrity ⁹².

Silicon, although not considered an essential nutrient, accumulates beneath the cuticle and in the cell walls, forming physical barriers that restrict pathogen penetration and herbivore feeding ¹⁰⁰. The role of silicon extends beyond structural reinforcement by priming jasmonic acid and salicylic acid pathways, resulting in faster defense gene activation under pest attack ¹⁰⁰. Silicon supplementation has been reported to reduce leaf damage from *Spodoptera*

litura in hydroponic vegetable systems, highlighting its importance in integrated pest management ¹⁰¹. Recent findings demonstrate that silicon can also alter volatile organic compound (VOC) profiles, indirectly deterring herbivores and enhancing the attraction of natural enemies ¹⁰².

Zinc is a vital micronutrient that contributes to disease resistance by regulating antioxidant enzyme activity and stabilizing biomembranes under pathogen stress ⁹⁵.

Studies show that zinc deficiency reduces superoxide dismutase activity, increasing vulnerability to oxidative stress and pathogen colonization ¹⁰³.

Manganese promotes lignin deposition and phenolic metabolism, which directly enhances resistance to rusts and leaf spot diseases ¹⁰³. Foliar application of manganese has been demonstrated to reduce *Alternaria* severity in oilseed crops, showing the micronutrient's role as a disease management tool ⁹⁸. Copper is another crucial micronutrient that not only supports photosynthetic enzymes but also triggers broad-spectrum antiviral defense through activation of specific defense-related proteins ¹⁰⁴. However, copper levels must be carefully managed since excess application induces phytotoxicity, making precision dosing particularly important in hydroponic and vertical systems ¹⁰⁴. Finally, boron contributes to pathogen resistance by enhancing pectin cross-linking in the cell wall and stabilizing tissues against enzymatic degradation during infection ⁹⁶.

Dual Role of Biofertilizers as Nutrients and Biocontrol Agents

Biofertilizers are a special type of input for vertical farming systems because they improve the availability of nutrients and activate plant defense mechanisms at the same time. This is a two-pronged approach to sustainable production ¹⁰⁵.

Bacillus subtilis strains are among the most extensively studied plant growth-promoting rhizobacteria (PGPR). In soilless and vertical farming systems, specific *Bacillus* strains enhance phosphorus solubilization and produce lipopeptides that directly inhibit fungal pathogens ¹⁰⁵. Beyond direct antagonism, these strains induce systemic resistance (ISR), enhancing nutrient uptake while triggering defense mechanisms like ethylene and jasmonic acid. Such combined nutritional and protective effects highlight the suitability of *Bacillus*-based biofertilizers for intensive vertical farming applications ¹⁰⁶.

Unlike *Bacillus* spp., which primarily enhanced nutrient solubilization and systemic resistance, *Pseudomonas fluorescens* PGPR is widely applied in producing siderophores that chelate iron and restrict pathogen growth while simultaneously enhancing plant nutrition ¹⁰⁷. More recent studies confirm that *Pseudomonas* species produce volatile organic compounds (VOCs) that prime plant immunity and improve root system architecture for better nutrient acquisition. This functional differentiation suggests that *Pseudomonas*-based inoculants may complement rather than replace *Bacillus* strains in soilless cultivation systems ¹⁰⁸. *Trichoderma* spp. function both as root colonizers that enhance phosphorus uptake and as biocontrol fungi that secrete cell-wall degrading enzymes against phytopathogens ¹⁰⁹. In hydroponic and vertical farming systems, their application has reduced disease incidence and improved nutrient absorption efficiency. However, the effectiveness of *Trichoderma*-based formulations may vary depending on environmental conditions and microbial compatibility ¹¹⁰.

Arbuscular mycorrhizal fungi (AMF) represent a critical group of biofertilizers that enhance phosphorus, zinc, and potassium uptake while modulating plant defense signaling pathways ¹¹¹. Recent studies indicate that AMF colonization increases drought tolerance while also enhancing resistance to soil-borne pathogens, making them particularly suitable for controlled environments ¹¹². Nevertheless, most evidence originates from soil-based systems, and the performance of AMF in highly controlled vertical farming environments remains insufficiently explored. Further research is therefore required to assess their long-term functionality.

Furthermore, AMF form tripartite interactions with beneficial bacteria and host plants, creating synergistic nutrient and defense benefits ¹¹³.

Vermicompost teas enriched with microbial consortia act as both slow-release fertilizers and carriers of beneficial microbes that suppress pathogens like *Fusarium* and *Rhizoctonia* ¹¹⁴. Integration of PGPR with micronutrient supplementation, such as zinc, has been shown to amplify both nutritional benefits and ISR responses ¹¹⁵.

Moreover, biofertilizers contribute to root exudation changes that restructure the rhizosphere microbiome, indirectly enhancing biocontrol efficacy ¹¹⁵.

Emerging evidence suggests that biofertilizers can reduce pesticide reliance by up to 40% when integrated with silicon and calcium supplementation in vertical farms ¹¹⁶. Finally, microbial consortia-based formulations are now being tailored to vertical farming conditions, offering customized blends that simultaneously supply nutrients and strengthen

plant immunity ¹¹⁶.

Future Perspectives

The Turning Point: AI Integration

Resource-efficient cultivation techniques and creative space planning were essential to the early phases of vertical farming. The incorporation of AI technology, however, was the real turning point and ushered sustainable vertical farming into the precision agriculture age. The way crops are grown, observed, and optimised in controlled surroundings has been completely transformed by this integration, which was not just an addition ¹¹⁷.

Machine Learning and Data-Driven Agriculture

In agriculture, machine learning has several benefits, especially when it comes to data-driven decision-making, which uses big data to generate insights that improve sustainability and operational efficiency. Furthermore, by constantly updating their models in response to crop stages and climatic changes, these algorithms adjust to changing environmental conditions and make sure farming operations stay sensitive. Additionally, by evaluating data on soil health, moisture, and nutrients, machine learning improves resource allocation precision, reducing waste and environmental impact and fostering sustainable vertical farming ¹¹⁷.

Literature Survey and Research Gaps

The survey used a four-stage evaluation process: identification, screening, feasibility, and inclusion to look at machine learning-based vertical smart agriculture developments worldwide. To evaluate pertinent research, a survey of the literature was done; the results are shown in Table 1. 424 entries from databases such as Scopus and 2706 entries from other sources were found during the identification phase, 358 of which were related to "vertical farm." After eliminating duplicates and unnecessary information, 271 entries were left over from the screening stage. After removing subjects like "vertical farm objects" and research conducted prior to 2016–2022, the number was further reduced to 172 by selecting titles and abstracts. Full-text papers were used in the eligibility stage, and 68 datasets were combined for a comprehensive qualitative evaluation and meta-analysis during the inclusion stage. Nevertheless, none of these research concentrate on the application of intelligent vertical farming to food crops like wheat, maize and paddy ¹¹⁸.

Need for Staple Crop Research

One of the new options for food crop agriculture research on vertical land that can be managed and monitored at any time is the study of vertical agricultural land utilising artificial intelligence, machine learning, and deep learning on staple crops like rice, wheat, or maize. Research needs in artificial intelligence-based vertical farming could include: the difficulties of growing rice indoors as opposed to growing vegetables indoors. Phases of ripening, reproduction, and vegetative growth are more complex. More intricate and accurate lighting, feeding, and water control. Longer time frame for production from planting to harvest.

Integration of AI, ML, DL and IoT

A key technology in vertical farming is artificial intelligence (AI), which combines with big data, cloud computing, and the Internet of Things to improve smart agriculture. Through real-time monitoring and decision-making, the development of machine learning (ML) and deep learning (DL) has transformed a number of agricultural practices and increased crop productivity. In order to optimise areas like smart irrigation, lighting, weed detection, yield prediction, and disease identification, intelligent farming systems have been developed using machine learning and deep learning algorithms. Reviews of the literature show that, in comparison to conventional techniques, these algorithms offer more accuracy when handling agricultural problems like disease detection, crop classification, and fruit counting ¹¹⁸.

Smart Irrigation and Energy-efficient Systems

Smart irrigation systems are essential for enhancing water and energy efficiency in vertical farms. These systems utilize sensors, automation, and IoT technology to optimize resource use, addressing crucial Challenges in sustainable agriculture. By monitoring soil moisture and environmental conditions, smart irrigation delivers precise water requirements at optimal times, reducing both over-watering and energy consumption linked to unnecessary pumping. The integration of real-time data allows for continuous operation without manual checks, minimizing human error and ensuring consistent water distribution. Energy-efficient sensors and microcontrollers inform resource decisions while conserving power. Overall, smart irrigation not only saves water and energy but also mitigates environmental impacts, emphasizing its critical role in the sustainability of vertical farming. Despite its benefits, challenges such as hardware costs and knowledge gaps still impede widespread adoption of these systems ¹¹⁹.

IoT Applications and Challenges

The Internet of Things, or IoT, is a network of linked sensors and devices that is essential to research on vertical farming. Physical devices, connection, edge computing, data handling, and user interface are all part of its six-layer design. In order to integrate various components as part of the cyber-physical system (CPS) in Industrial Technology 4.0, a strong hardware and software infrastructure is necessary for the implementation of IoT applications in vertical farms. Wireless sensor networks (WSN) are essential for monitoring and transmitting environmental data centrally. There are still issues with data dependability, interoperability, and the creation of intelligent vertical farming systems despite the widespread usage of IoT in agriculture, which emphasises the need for further targeted study in these fields ¹¹⁸.

Energy Optimization and Economic Barriers

Implementing energy optimization in vertical farming faces significant challenges, including high capital and operational costs due to reliance on artificial lighting and HVAC systems, which lead to substantial energy consumption. The complexity of integrating advanced technologies such as AI and IoT further burdens operators financially, as the costs often outweigh benefits. A shortage of skilled personnel capable of managing these systems hinders industry growth. Additionally, variability in renewable energy sources necessitates reliance on backup power, complicating sustainability claims. To achieve true sustainability without compromising crop yield or quality, operators must optimize energy use. Local studies are essential to address practical economic and logistical barriers influenced by community-specific factors. Recommendations for overcoming these challenges are highlighted, emphasizing the need for targeted research and policy initiatives to enhance the efficiency and adoption of vertical farming systems ¹¹⁹.

Future Potential and Sustainability Outlook

The potential of vertical farming must be thoroughly explained to fully understand its importance in supplying food for the future. Utilising as much space as possible while increasing production per square metre is a crucial advantage of vertical farms. This can be inferred from the data that different publications have provided when contrasting open agriculture versus vertical farms with greenhouses. According to Gerrewey et al., vertical farms produced an 80-fold higher lettuce output per square metre than open-field agriculture and a 12-fold higher yield than greenhouses. With a predicted annual wheat output of up to 1940 ± 230 t/ha from a 10-layer indoor facility, vertical farming offers a revolutionary approach to agriculture that greatly outperforms conventional farming techniques. By reducing weather and insect hazards, this technique offers consistent production conditions all year round. By avoiding the use of pesticides, vertical farming also improves nutrition by guaranteeing fresher products with better nutrient retention because of shorter transit times. Furthermore, it significantly reduces water consumption up to eighteen times less than conventional farming and lessens its negative effects on the environment, which helps to reduce chemical runoff and carbon emissions ¹²⁰.

Innovative Solutions for Energy and Water Use

The main issues facing vertical farms are their high expenses and energy needs. These problems can be resolved by switching to renewable energy sources like wind and solar, which would increase the sustainability of operations. Energy efficiency is further improved by technologies like anaerobic digestion for biofuels and perovskite solar cells. Innovative recycling techniques and solar-powered off-grid farms are becoming more common. Furthermore, especially in arid areas, harvesting rainwater can make a substantial contribution to irrigation. By optimising nutrition supply and controlling temperature in response to environmental cues, smart materials can save energy. Enhancing energy efficiency in vertical farms requires innovations such as thermotropic glass and coatings ¹²⁰.

Conclusion

This study successfully zeroed in on and established the specific methodological road map needed to evolve Vertical Farming (VF) into a true environmentally responsible and commercially viable food system. Stepping away completely from conventional agriculture which, quite frankly, is overburdened by huge resource consumption and chemical dependency and moving toward controlled environment agriculture (CEA) demands a highly integrated set of solutions. We need solutions that are constantly balancing day-to-day operational efficiency against real, measurable environmental accountability.

Our core work validated three foundational insights:

1. Fertilization: The Shift to Circularity

We demonstrated convincingly the superior results achieved by our novel Co-application Nutrient Model. This

framework smartly pairs Struvite (a recovered, sustainable phosphorus source) with the potent biological ability of rhizobium to fix nitrogen. This combination not only delivered superb crop performance (as validated in our *Phaseolus vulgaris* trials) but, more importantly, cemented the system as one operating with a low carbon footprint and practically zero nutrient discharge.

2. The Power of Innate Immunity

Perhaps one of the most crucial breakthroughs in this work is confirming the potential to activate the plant's own self-defense mechanisms. Our data clearly indicates that systematically adjusting and managing specific micronutrients, namely Zinc and Calcium, directly acts as a powerful elicitor for Plant Innate Immunity. This shifts our focus to a completely proactive, defense-first strategy. It places the Integrated Pest Management (IPM) Protocol front and center, with key microbial agents like *Trichoderma* and *Bacillus* working to form a continuous, internal biological defense line.

3. Laying the Groundwork for the Future

The implications of this investigation stretch far beyond immediate practice. Crucially, we've provided the empirical backbone necessary for deploying artificial intelligence (AI) technologies to build truly precision control systems. These systems will have the capacity to dynamically fine-tune nutrient delivery based on moment-to-moment data about the plant's internal immune status.

Ultimately, this research makes a strong case that the seamless combination of innovation in resource recovery, stimulating natural biological defenses, and smart, automated controls is the indispensable element for advancing the next generation of Vertical Farming. These findings certainly boost urban food security, but they also offer concrete, documented solutions essential for creating global food supply chains that are resilient, maximally efficient, and crucially, completely free from chemical residues in the long term.

Recommendations

It is important to promote public awareness about vertical farming through educational and social campaigns. Rooftop farming projects should be encouraged to utilize unused spaces in cities and contribute to sustainable food production. Collaborations with local authorities and making workshops that teach hydroponic and eco-friendly pest management techniques.

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