

## Advanced Formulation and Controlled Delivery Technologies for Stress-Mitigating Bioactive Agents

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### Abstract

Advanced formulation and controlled delivery technologies are increasingly critical for improving the stability, bioavailability, and functional performance of bioactive agents under complex biological environments. In agriculture, climate change intensifies the frequency and severity of abiotic stresses (drought, salinity, temperature extremes, flooding) and biotic pressures (pathogens, pests), creating compound stress conditions that challenge conventional agrochemical inputs characterized by low use efficiency and high environmental losses. This review synthesizes recent advances in stress-mitigating bioactive agents including plant hormones and signaling molecules, melatonin, seaweed-derived extracts, microbial biostimulants such as plant growth-promoting rhizobacteria (PGPR), and protective metabolites like polyamines through the lens of formulation science and controlled delivery. Plant stress-response mechanisms involving immune signaling (PTI/ETI), hormonal crosstalk (notably ABA–JA interactions), and reactive oxygen species (ROS)-mediated redox regulation are discussed to provide a mechanistic basis for delivery system design. Emerging formulation strategies based on biodegradable polymers, microencapsulation, nano- and microstructured carriers, and hydrogel matrices demonstrate improved cargo protection, tunable release kinetics, and reduced off-target dispersion. Controlled and targeted delivery approaches including stimuli-responsive platforms, pH-responsive sustained-release hydrogels, foliar uptake with systemic translocation, and biorecognition-based targeting enable synchronization of bioactive release with physiological demand and environmental cues. Evidence from meta-analyses indicates that biologically based inputs and controlled-release fertilizers enhance stress tolerance, stabilize yields, improve nutrient use efficiency, and reduce nitrate leaching. Collectively, integrating bioactive agents with advanced delivery technologies establishes a framework for precision-guided, resource-efficient, and environmentally responsible input design, positioning agricultural systems as a valuable platform for advancing controlled delivery science.

**Keywords:** biostimulants; controlled release; nanocarriers; plant stress tolerance; sustainable agriculture

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### 1. Introduction

The global agricultural systems are becoming threatened by ever-increasing pressures of climate change and environmental stress factors. There is a rich spectrum of abiotic stresses to which crop plants are often subjected (drought, salinity, temperature extremes, and flooding) in addition to biotic ones (pathogens and pests). Notably, the stresses are normally experienced either in a synergistic or sequential manner that

produces multifaceted stress conditions that interfere drastically with plant development, physiology, and the formation of yield. Abiotic and biotic stresses may stimulate each other thus causing higher yield penalties than those resulting due to the presence of either stress factors in isolation<sup>1</sup>. These combinations of stresses are an important threat to the global food security and agricultural sustainability.

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Global analysis has shown clearly that crop production systems are susceptible to climatic variations and catastrophic weather patterns. Examining past records has revealed that droughts, heatwaves and floods have already resulted in significant crop losses in the world, especially in the major cereal-producing areas<sup>2</sup>. Agroecosystems are likely to be further exposed to these risks due to climate change, which is likely to increase the frequency and severity of extreme climatic events, and will impose additional stress upon agroecosystems already under pressure<sup>3</sup>. According to the recent findings, the negative effects of climate change on crop yields can be underestimated significantly because a number of predictive models do not provide the complete picture on the effect of the compound stress and complicated crop reactions<sup>4</sup>. Thorough reviews have also pointed out that yield cuts will become severe in changes of climate in the future, and there is an urgent need of creative solutions to strengthen crop resistance<sup>5</sup>.

Conventional farming methods have used synthetic fertilisers and pesticides as a major way of alleviating losses in yields related to stresses. Although these inputs have brought yield gains in the past, their long term usefulness is being increasingly challenged with poor use efficiency, rapid degradation and loss through leaching, besides causing adverse impact on environment. The overuse of agrochemicals may lower the quality of soil, interfere with the favorable microbial microflora, and cause environmental pollution. This has led to an increasing interest in alternative, sustainable ways of making crops more resistant to stress with having minimal effects on the ecology.

In this regard, bioactive agents that mitigate stress have been developed as an important tool to enhance the resistance of plants to unfavorable environmental factors. These actors are plant hormones, signaling molecules, biostimulants and extracted natural compounds that influence physiological, biochemical and molecular stress responses. Bioactive agents have the ability to augment antioxidant defense mechanism, regulating hormonal equilibrium, enhancing nutrient assimilation, and stabilizing the cell construction during stress. Of these, biostimulants have gotten significant focus because of their capacity to enhance the performance of plants without necessarily providing nutrients to them. It has been demonstrated in recent research that biostimulants have the ability to boost tolerance to abiotic stresses through the enhancement of photosynthetic efficiency, water-use efficiency, and stress-responsive metabolic pathways<sup>6</sup>.

Melatonin and other specific bioactive compounds and their multifunctional roles in the tolerance to plant stress have been extensively studied. Melatonin is a growth regulator, biostimulator, which is important in reactive oxygen species (ROS) scavenging, hormonal regulation, and activation of stress-defense mechanisms. Its use has been demonstrated to enhance drought, salinity, and temperature tolerance of plants, which is why it may be used as a useful stress-reducing agent in agriculture<sup>7</sup>. Although the above advantages of bioactive agents were illustrated, these agents are usually limited in their practicality in the field setting due to their low stability, low bioavailability, rapid degradation, and poor delivery to their target plant tissues.

To solve these predicaments, the science of formulation and controlled delivery technologies have become more and more significant in contemporary agriculture. Sophisticated approaches in formulation are used to safeguard bioactive agents against degradation in the environment, improve their solubility, and provide control of release or their release in a neurotrophic activity. Controlled release formulations have already been utilized effectively in the delivery of pesticides where they have yielded better efficacy, less application frequency and less environmental hazards as compared to

traditional formulations<sup>8</sup>. Such innovations offer a good basis in the establishment of effective transport methods of stress-relieving bioactive substances.

Agricultural bioactive agent delivery systems based on nanotechnology are one of the most promising avenues of enhancing the performance of bioactive agents. The benefits of nano-enabled formulations, such as nanofertilizers, are controlled and slow release of active compounds, increased nutrient use efficiency and improved plant uptake. Recent research has established that nanofertilizers are able to boost the crop yields and minimize loss of nutrients and environmental pollution<sup>9</sup>. Moreover, it was also demonstrated that nanomaterials can stimulate plant growth and resistance to abiotic stresses, improve physiological processes and stress-responsive pathways, which makes them one of the primary building blocks of a new generation of sustainable agricultural systems<sup>10</sup>.

Altogether, the combination of the bioactive substances that reduce the impact of stress factors with the sophisticated formulation and controlled delivery regimes is a potent solution to improving the tolerance of crops to the impact of the growingly stressful environmental factors. The synergistic nature between bioactive compounds and delivery systems is an important area of understanding required to come up with effective, targeted agricultural inputs, which are environmentally responsible. The objectives of the study are:

1. To access stress-mitigating bioactive agents and their roles in enhancing crop tolerance under abiotic and biotic stresses
2. To assess formulation and controlled delivery strategies that improve the effectiveness of agricultural bioactive agents; and
3. To evaluate the impact of advanced delivery systems on crop performance and agricultural sustainability.

## 2. Plant Stress Factors and Crop Response Mechanisms as Delivery-Relevant Biological Microenvironments

Crop plants are subjected to the broad range of environmental stresses that have adverse effects on growth, development, and productivity. These stressors consist of the abiotic stresses, drought, salinity, extreme temperatures, and the oxidative stress and the biotic stresses of microorganisms and others that cause pathogens and pests. According to the controlled delivery view, the conditions of these forms of stress determine highly dynamic biological micro environments, with variation in pH, redox status, enzymatic activity, and hormonal signaling. In this regard, knowledge about plant stress-response mechanisms is crucial not only in the improvement and enhancement of crop stress-tolerance but also in rationally tailoring formulation and delivery systems that react to biological and environmental cues. Regarding controlled delivery, highly dynamic biological microenvironments are characterized by plant stress conditions that have a direct effect on carrier behavior, cargo stability and release kinetics. The differences in pH, redox potential, enzymatic activity, tissue permeability, and hormonal signaling in abiotic and biotic stress provide endogenous stimuli to be utilized in stimuli-responsive and targeted delivery. Knowledge of plant stress-response mechanisms is thus vital to enhancement of stress tolerance, as well as to the rational design of delivery systems that can release at the site and timing and in response to demand

### 2.1 Biotic Stress Responses and Plant Immune Signaling

Plants have an inbuilt immune system which can help to respond quickly to the invading pathogens. Pattern-triggered immunity (PTI) begins by the recognition of conserved pathogen-associated molecular patterns (PAMPs) by pattern recognition receptors (PRRs) found on the surface of plant cells. The activation of PTI causes calcium influx, calcium-calcium signaling (MITO) cascades, and massive

transcriptional reprogramming, which results in the expression of defense-related genes<sup>11</sup>. The signaling of these immune-associated events comes with local biochemical alterations that can be used as internal signaling of stimuli-responsive delivery systems.

A type of immunity, effector-triggered immunity (ETI) occurs when the intracellular immune receptors detect the presence of pathogen-derived effector proteins. As opposed to operating independently, PTI and ETI work jointly using coupled signaling networks that reinforce and renew immune responses<sup>12</sup>. PTI-ETI crosstalk expression produces distinct molecular phenotypes, such as increased redox capacity and enzymes activation, which are becoming important in the design of biorecognition-based and immune-triggered delivery platforms.

### 2.2 Abiotic Stress Factors and Hormonal Regulation

Drought is one of the most relevant limitations of crop productivity among other abiotic stresses. Stressors such as drought cause physiological and molecular changes to achieve water conservation and cellular homeostasis. The central part in these responses is played by Abscisic acid (ABA) which has the ability to control stomatal closure, osmotic adjustment and expression of stress-responsive genes<sup>13</sup>. In the context of delivery, ABA-controlled processes change the permeability of the tissues, rates of transpiration, and transportation routes and thus affect bioactive agent uptake and distribution.

Heat and cold are some of the temperature stresses that interfere with cellular structures and metabolism. Transcriptional and post-transcriptional networks that are complicated in regulating plant responses to drought and cold stress include stress-responsive transcription factors, protein kinases, and epigenetic regulators<sup>14</sup>. Such regulatory control systems create heterogeneity in space and time in plant tissues, and the significance of controlled and sustained release systems that can preserve bioactive availability at varying environmental conditions.

### 2.3 Reactive Oxygen Species and Oxidative Stress Signaling

Reactive oxygen species (ROS) have a two-fold effect on plant stress responses as signals in controlled conditions but lead to oxidative damage in excessive conditions. Abiotic stressors like drought, salinity, temperature extremes, and others may increase the levels of ROS, which results in lipid peroxidation, oxidation of proteins and nucleic acids. Plants have enzymatic antioxidants such as superoxide dismutase, catalase, and peroxidases and non-enzymatic antioxidant systems<sup>15</sup> to counter oxidative stress.

### 2.4 Hormonal Crosstalk Between Abiotic and Biotic Stress Responses

Abiotic and biotic stress responses in plants are interconnected by an elaborate hormonal crosstalk between abscisic acid, salicylic acid, jasmonic acid and ethylene. The two hormones cooperate to tune stress-specific signaling pathways, as well as strike a compromise between the growth and defense requirements<sup>16</sup>. This type of hormonal integration forms context-sensitive signaling landscapes, which are capable of determining the timing, localization, and efficacy of delivered biologically active agents.

As an example, the abiotic stress tolerance is mediated mainly by ABA, and the biotic defense responses are controlled by salicylic acid and jasmonic acid. Such interactions can either be synergistic or antagonistic depending on the environmental conditions and it is therefore important to have a delivery system that is selective to certain hormonal or enzymatic signals. The knowledge of hormonal crosstalk can thus give a mechanistic basis of designing specific precision delivery plans in line with complex stress situations.

All in all, interdependent immune signaling, hormonal control, and redox interactions are interconnected that determine the biological background of bioactive delivery. The representation of these mechanisms as dynamic delivery-relevant micro environments offers a pivotal base on the development and controlled delivery strategies as discussed later. Table 1 is a summary of key plant stress-response mechanisms as delivery-relevant biological microenvironment, key biological signaling pathways and the implication of designing controlled, stimuli-responsive, and targeted delivery systems of agricultural bioactive agents.

**Table 1: Plant stress factors and core response mechanisms**

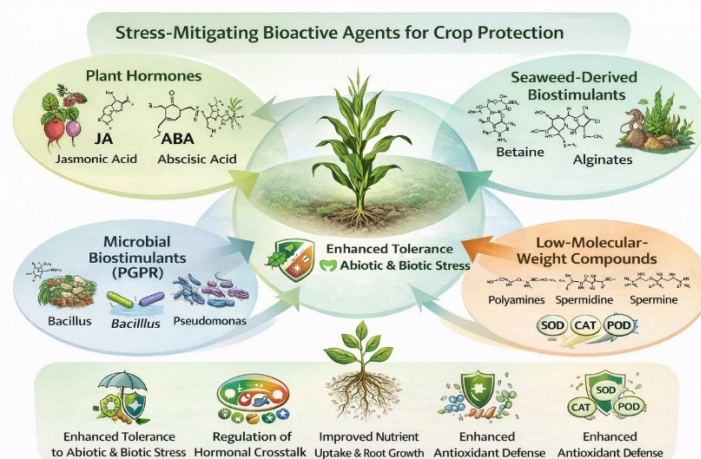
Stress type	Key signaling components	Major physiological responses	Source
Biotic stress (PTI)	PRRs, Ca <sup>2+</sup> influx, MAPK cascades	Basal immune activation, restriction of pathogen growth	[11]
Biotic stress (ETI)	NLR receptors, amplified defense signaling	Strong and durable immunity, defense gene induction	[12]
Drought stress	ABA signaling, stomatal regulation	Water conservation, osmotic adjustment, stress gene expression	[13]
Drought & cold stress	Transcription factors, kinase networks	Rapid gene reprogramming, cellular protection	[14]
Oxidative stress	ROS production and scavenging systems	Redox signaling, antioxidant defense activation	[15]
Hormonal crosstalk	ABA-SA-JA-ET interactions	Growth-defense balance, integrated stress response	[16]

### 3. Stress-Mitigating Bioactive Agents for Crop Protection

Biological active compounds that reduce stress have been receiving growing interest as a sustainable means of improving the resistance of crops to negative environmental factors. Bioactive agents operate by regulating internally based plant physiological and molecular pathways, similar to the action of conventional agrochemicals, unlike the latter which are mostly directed at external stressors and thus enhance intrinsic stress tolerance systems. Such agents include plant hormones and signaling molecules, natural and microbial biostimulants and low-molecular-weight protective domesticated compounds that jointly control growth-defense balance and stress adaptation. The key classes of stress-

reducing bioactive agents, e.g., plant hormones (jasmonic acid and abscisic acid), seaweed-derived biostimulants, microbial biostimulants (PGPR), and low-molecular-weight compounds (polyamines), and how these work together under combined abiotic and biotic stress to improve crop tolerance by crosstalk through hormonal signal transduction are shown in Figure 1. The mitigating bioactive agents on stress can be theoretically perceived as functional cargo molecules, the efficacy of which is determined by not only intrinsic biological activity but also efficiency of delivery and stability and bioavailability. The placement of agricultural bioactive agents in a paradigm of delivery science is able to systematically translate drug delivery concepts to agricultural systems and facilitate the

application of precision-controlled and environmentally accountable technologies of delivering inputs.



**Figure 1: Stress-Mitigating Bioactive Agents and Their Integrated Roles in Enhancing Crop Tolerance**

### 3.1 Plant Hormones and Stress Signaling Molecules

Plant hormones are crucial in the process of coordinating the plant reactions to abiotic stresses using complex networks of interactions. Jasmonic acid (JA) has become a dominant controller of stress tolerance in plants especially in cases of drought, salinity and temperature. JA helps in stress adaptation by increasing the antioxidant activity, maintenance of the accumulation of osmolytes and modification of the stress response gene expression. Notably, JA is not working in isolation, but it represents a broad crosstalk with abscisic acid (ABA), a central hormone in response to abiotic stress. JA-ABA interaction allows the stomatal behavior, water-use performance, and stress signal levels to be regulated finely and to permit plants to optimize their survival in response to changing environmental conditions<sup>17</sup>. This hormonal combination highlights why exogenous hormone-based bioactive agents, in a controlled manner, have a potential to increase stress tolerance levels.

### 3.2 Seaweed-Derived Biostimulants

The seaweed-based biostimulants form one of the most popular groups of natural bioactive compounds applied in the field of sustainable agriculture. These extracts contain a high concentration of bioactive constituents, such as polysaccharides, phytohormones, amino acids, and micronutrients in which their combined effect boosts the growth and stress tolerance of plants. Recent extensive reviews have shown that biostimulants derived by using seaweed are effective in improving crop tolerance to both abiotic and biotic stresses through a mechanism of increasing photosynthetic efficiency, nutrient uptake, and antioxidant defense systems<sup>18</sup>.

Molecularly, it has been demonstrated that seaweed extracts regulate hormonal balance and the induction of stress-responsive metabolic processes to prepare plants to better cope with stress. They are used to increase the resilience of plants to drought, salinity, and seasonal temperature, as well as to the resistance to the attack of pathogens<sup>19</sup>. Being naturally sourced, biodegradable, and posing a minimal threat to the environment, seaweed-derived biostimulants are an important ingredient of the biologically friendly crop management practices.

### 3.3 Microbial Biostimulants and Plant-Microbe Interactions

Microbial biostimulants, more specifically the plant growth promoting rhizobacteria (PGPR) are very important in helping

to improve the tolerance of plants to stress through the exploitation of positive plant-microbe interactions. These microorganisms enhance the performance of plants by assisting the process of acquiring nutrients, synthesis of phytohormones and triggering of systemic tolerance defense. On a physiological and molecular scale, microbial biostimulants also increase root system architecture, stress-responsive gene expression, antioxidant capacity, and plant stress resilience<sup>20</sup>.

PGPR use a variety of different mechanisms to promote plant growth in deplorable conditions, such as nitrogen fixation, solubilization of phosphates and the generation of bioactive metabolites. They also affect hormonal signaling pathways including auxins, ABA, and ethylene, which helps plants to be more resistant to abiotic stresses but allow them to grow<sup>21</sup>. The idea of integrating microbial biostimulants into crop production is a prospective strategy towards cutting back on synthetic inputs and maintaining productivity in stressful situations caused by changes in the climate.

### 3.4 Polyamines and Other Protective Bioactive Compounds

Polyamines are small polycationic molecules that play multifunctional roles in plant growth and stress tolerance. They contribute to stress mitigation by stabilizing cellular membranes, scavenging reactive oxygen species, and regulating gene expression under adverse conditions. Recent studies have highlighted the role of polyamines in enhancing tolerance to drought, salinity, and temperature stress through their involvement in redox homeostasis and hormonal crosstalk<sup>22</sup>.

Polyamines also interact with other bioactive compounds and signaling molecules, contributing to the coordinated regulation of stress responses. Their ability to integrate antioxidant defense, hormonal regulation, and metabolic adjustment makes them promising candidates for inclusion in stress-mitigating formulations aimed at enhancing crop resilience. Overall, stress-mitigating bioactive agents represent a diverse and powerful toolkit for improving crop tolerance to environmental stresses. By modulating hormonal signaling, enhancing antioxidant defenses, and strengthening plant-microbe interactions, these agents contribute significantly to sustainable crop protection.

## 4. Formulation Strategies for Agricultural Bioactive Agents

Formulation of stress-reducing bioactive agents is also of great importance in their use in agricultural systems. Although bioactive compounds like biostimulants, hormones and protective molecules have great potential of improving crop tolerance, their practical usage is usually limited by instability, low solubility, degradation and uncontrolled distribution to the environment. As a result, formulation planning is very important in enhancing stability, bioavailability, and delivery of agricultural bioactive agents. Figure 2 demonstrates traditional and new development strategies of agricultural bioactive agents. Whereas the traditional solutions and

granules provide rapid release but poor in the aspects of stability and environmental losses, the polymer-based systems, nano-/microstructured carriers, and smart microencapsulation enhance stability, controlled release, delivery efficiency and environmental safety that assists crop production in a sustainable manner.

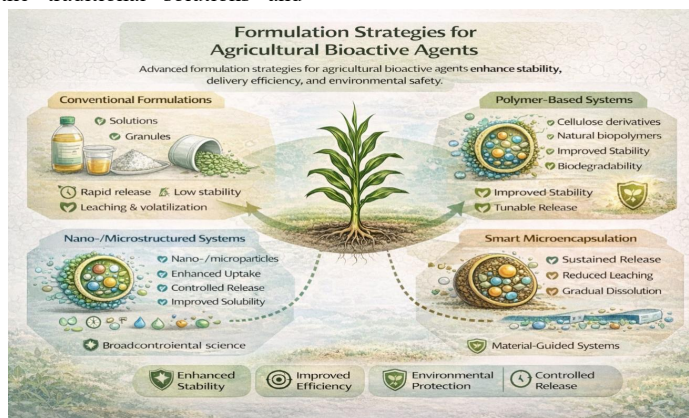


Figure 2: Formulation Strategies for Enhancing Stability and Delivery of Agricultural Bioactive Agents

#### 4.1 Conventional Formulation Approaches and Limitations

The conventional agricultural inputs are usually in the form of liquid solutions, emulsifiable concentrates, wettable powders, and granular products. These formulations are very popular because of their simplicity and low cost, but they are usually affected with a number of shortcomings. It can have a short effect as rapid release of active ingredients causes short-term effectiveness, whereas environmental factors (light, temperature, and moisture) increase degradation rate. Moreover, uncontrolled release causes more risk of leaching, volatilization and off-target effects which contribute to loss of efficacy and environmental pollution.

These constraints are especially problematic in the case of bioactive agents that tend to work at low doses and time and space specificity in order to induce stress-mitigation pathways. Consequently, traditional equations often cannot provide a steady and long-term benefit in the field conditions, which leads to the necessity of innovative approaches to formulation.

#### 4.2 Polymer-Based Formulation Systems

The materials made of polymers have become very effective platforms toward enhancement of formulation of agricultural bio active agents. Cellulose based materials are particularly appealing among them because of their biodegradability and renewability, along with the chemical versatility. Derivatives

of modified cellulose have been widely developed as the controlled-release formulation of agrochemicals, with enhanced encapsulation capacity, controllable release rate, and environmental friendliness<sup>23</sup>. Cellulose-based carriers can be designed to react to environmental factors, e.g. moisture and pH, by chemical modification, to allow controlled release of active compounds.

Originally natural polymers are also becoming favourable in the encapsulation of biostimulants in order to offer them protection against degradation and enhance functional performance. Biopolymers encapsulation increases the stability of bioactive compounds, shelf life, and gradual release and, therefore, boosts their efficacy in the conditions of stress<sup>24</sup>. These methods are especially applicable to sensitive bioactive agents which deteriorate quickly when used in standard formulations. The summary of the major strategies of formulation of agricultural bioactive agents, including the essential materials in use, the essential functional role of these materials, and the representative sources are summarized in Table 2. The comparison presents the shift of traditional formulations in terms of high rate of availability and low stability, to a new system, such as polymers, nano-/microstructured, microencapsulation, and material-guided, formulations aimed at improving the stability, controlling the release, bettering the delivery efficiency, and minimizing the environmental losses.

Table 2: Formulation strategies for agricultural bioactive agents

Strategy	Key materials	Core function	Source
Conventional formulations	Solutions, powders, granules	Rapid availability, low stability	[23]
Polymer-based systems	Cellulose, natural biopolymers	Improved stability, tunable release	[24]
Nano/micro-structured systems	Nano- & microparticles	Enhanced uptake, controlled kinetics	[25]
Microencapsulation	CMC microcapsules	Sustained release, reduced losses	[26]
Material-guided concepts	Membrane-inspired systems	Controlled transport, safety	[27]

#### 4.3 Nano- and Microstructured Formulations

The latest breakthroughs in the field of nanotechnology allowed the release of the nano- and microstructured formulation systems that provide a better means of control over the delivery of agricultural inputs. The nano- and

microstructured carriers enhance the surface area per interaction with the plant tissues, improve the solubility of poorly soluble compounds, and provide the possibility of precise control of the release kinetics. Inventions in this direction have shown high efficiency and sustainability in the

use of agricultural inputs in the sense of fertilizers, pesticides and biostimulants<sup>25</sup>.

Nano- and microstructured systems can also offer alternative possibilities of targeted delivery, minimizing the required active ingredient, and leading to a minimum ecological loss. Through particle size, morphology, and surface property these systems can be optimized to maximize soil and root surface/foiar tissue interaction and thus increase uptake and bioavailability.

#### 4.4 Smart Microencapsulation and Controlled Release Formulations

Microencapsulation is one of the most significant approaches to formulation that was to be employed to get the bioactive agents under the control with sustained release. Microcapsules using carboxymethyl cellulose (CMC) as an example have been used to successfully design smart delivery of pesticides, which present less dangers to the environment due to controlled delivery and reduced environmental leaching<sup>26</sup>. These types of microcapsule systems help to shelter active components against early degradation and release active components over time in a gradual way that will guarantee the effects are felt over a long period.

Finally, advanced formulation strategies are associated with the enhancement of the efficiency of the delivery process as well as larger sustainability objectives. Indicatively, in the example of membrane-based technologies, in spite of the fact that their main use is in environmental remediation, it is emphasized that the design of materials determines the rates of transport and release<sup>27</sup>. By considering insights of such technologies the formulations of agriculture that minimize unwanted environmental distribution of active compounds can be developed.

On the whole, the use of the advanced formulation strategies, especially those involving the use of biodegradable polymers, nano- and microstructured systems, and smart encapsulation technologies, is necessary to maximize the efficacy of stress-reducing bioactive agents. Such strategies do not only improve stability and delivery effectiveness but also help to minimize environmental risks and hence the shift to more sustainable and resilient agricultural systems.

#### 5. Advanced Delivery Systems: Nano- and Polymer-Based Approaches

However, new nanotechnological and polymer science based advanced delivery systems have become innovations in enhancing efficiency, accuracy and sustainability of agricultural inputs. Even traditional preparations cannot provide bioactive agents in controlled and targeted form, which reduces their efficiency and causes more losses to the environment. These shortcomings can be overcome using nano- and polymer-based delivery systems that improve the

stability, bioavailability, and controlled delivery of stress-reducing bioactive factors.

#### 5.1 Chitosan-Based Nanoparticle Delivery Systems

Chitosan nanoparticles are among the biopolymer-based nanocarriers which have drawn significant interest because of their biodegradability, biocompatibility, and their bioactivity property. Delivery systems made of chitosan have several functional benefits such as high encapsulation efficiency, active compounds are not degraded and controlled release behavior. Chitosan nanoparticles in agriculture have been demonstrated to enhance the use of agrochemicals and bioactive agents and have been found to decrease environmental pollution<sup>28</sup>.

Other than their carrier role, chitosan nanoparticles may also cause plant defense responses, which act synergistically in tolerance to stress. Their positive charge promotes bonding with the negatively charged surfaces of plants and thereby making the adhesion and uptake easier. All these characteristics allow chitosan-based nanocarriers to be especially appropriate in the delivery of stress-reducing agents in sustainable agricultural systems.

#### 5.2 Lignin Nanoparticles as Sustainable Carriers

Lignin nanoparticles have become potential, renewable delivery systems to agriculture. Lignin, which is a by-product of the large amounts of vegetal biomass, has natural antioxidants, UV protection, and biodegradability. The other recent developments in the preparation and characterization of lignin nanoparticles prepared using different sources of plants have shown their structural diversity and applicability to encapsulation applications<sup>29</sup>.

Nanocarriers made of lignin can be utilized to shield vulnerable bioactive agents against photodegradation and oxidative degradation and increase their useful life in the field. Moreover, targeted delivery and minimized off-target are achieved by the fact that the tunable surface chemistry of the lignin nanoparticles can be used to control interactions with plant tissues and soil, increasing targeted delivery and reducing unintended side effects. These characteristics make lignin nanoparticles promising substitutes of synthetic nanoparticle materials in sustainable farming. Table 3 characterizes the main nano- and polymer-based delivery platforms that have been created to deliver agricultural bioactive agents with an emphasis on carrier materials and their main functional characteristics. These systems such as chitosan and lignin nanoparticles, biomedical-inspired controlled release matrices, and polysaccharide-based hydrogels can lead to better encapsulation, controlled and stimulus-responsive release, stability improvement, and reduced environmental losses, and can facilitate efficient and sustainable delivery of stress-reducing inputs in crop production.

**Table 3: Nano- and polymer-based advanced delivery systems for agricultural bioactive agents**

Delivery system	Carrier material	Key functional properties	Source
Chitosan nanoparticle systems	Chitosan (biopolymer)	Biodegradable, cationic surface, high encapsulation efficiency, controlled release	[28]
Lignin nanoparticle carriers	Lignin (plant-derived polymer)	Antioxidant activity, UV protection, tunable surface chemistry	[29]
Biomedical-inspired controlled release systems	Polymer matrices, stimuli-responsive carriers	Diffusion-controlled release, matrix degradation, environmental responsiveness	[30]
Polysaccharide-based hydrogel systems	Natural polysaccharides	High water retention, sustained release, biodegradability	[31]

#### 5.3 Translating Controlled Release Concepts from Biomedicine

The agricultural delivery systems have received important lessons with the controlled release technologies that were first

developed in the field of biomedical use. Diffusion-controlled release, matrix degradation, and stimulus-responsive behavior, among others, can be translated to suit the requirements of the particular environment of agriculture. The translational

research has emphasised the potentials of delivery platforms in the biomedical system to enhance the accuracy and effectiveness of delivering agrochemicals and bioactive agents<sup>30</sup>.

Through the conceptualization, it is possible to design agricultural delivery systems to react to environmental signals, including moisture levels, pH, or enzymatic activity, and release them at the point of deposition site-specifically and time-dependent. This will reduce losses of active ingredients and will improve stress-mitigation effects especially in dynamic field conditions.

#### 5.4 Polysaccharide-Based Hydrogel Delivery Systems

Hydrogels made of polysaccharides are a sophisticated type of polymer-based carrier, which can hold a high volume of water at the same time allowing release of the contents in the capsule to be regulated. Natural polymers have been produced into sustainable hydrogel spheres that have been shown to have controlled release of agricultural inputs such nutrients and bioactive compounds<sup>31</sup>.

These hydrogel systems offer a longer duration of the availability of active agents, less leaching losses, and better coordination between the dynamics of release and the demands of the plant. They are also biodegradable and compatible with soil ecosystems which also increases their suitability to sustainable agricultural use. Hydrogel-based carriers, when used in the presence of stress-inducing factors, have the potential to enhance the ability of water to retain and deliver into the crops at a slow and constant rate stress-reducing bioactive agents, thus increasing crop resilience.

In general, nano-delivery systems and polymer-based delivery systems provide potent platforms to enhance the functionality of agricultural bioactive agents. These advanced systems are highly effective in the delivery process since they combine biodegradable materials, controlled release, and targeted delivery methods to ensure that the delivery is more efficient with minimal environmental risks. Their further creation and optimization are vital to the further development of sustainable and resilient practice of agriculture.

### 6. Controlled Release and Targeted Delivery Mechanisms

The delivery and release of stress-reducing bioactive agents in the contemporary agriculture sector have been unlocked through controlled release and delivery mechanisms. Although advanced carriers have enhanced loading capacity and stability, the real agronomic benefit can be observed in the regulation of the release of bioactive agents in terms of the timing, location, and manner. Delivery that is not well controlled is likely to lead to premature degradation, leakage, and off-target accumulation, lowering efficacy and posing a high environmental risk. However, in contrast, controlled and targeted delivery systems coordinate bioactive release to plant physiological requirements and environmental signals to achieve the maximum of stress-mitigating and resource-use efficiency.

#### 6.1 Stimuli-Responsive Delivery Systems

Stimuli-responsive delivery systems will be a significant technological breakthrough in precise agriculture. The systems are done to emanate active compounds regarding certain environmental or biological indicators like pH, wetness, heat, redox potential, or enzymatic activity. Stimulus-responsive nano-based pesticides have shown great prospects of enhancing precision in delivery and reducing unneeded exposure to the environment<sup>32</sup>. These systems are functional because by allowing activating bioactive agents on demand, they can be activated only when the conditions are stress-relevant, which in turn improves their usefulness.

The use of polymer stimulus-responsive carriers also enhances the capability of the controlled release platform. Rational polymer design and functional group modification make release kinetics fine-tuning to react to the changes of the microenvironment in the soil or plant tissues. These types of systems enable the prolonged and controlled dispersion of agrochemicals and bioactive agents, lowering the application rate and avoiding dangers of excessive use<sup>33</sup>. Notably, the stimuli-responsive carriers match the sustainability objectives of the delivery technology by minimizing the use of chemicals even though they do not compromise agronomic performance.



**Figure 3: Controlled Release and Targeted Delivery Mechanisms in Agriculture**

Figure 3 illustrates key delivery strategies to stress-reducing bioactive agents which are stimuli-responsive delivery, pH-responsive hydrogels, foliar delivery with systemic translocation and targeting using bioreceptors. These strategies improve precision of delivery, allow release to be sustained as well as on command and minimize losses in the environment which increases stress tolerance and sustainability in crops.

#### 6.2 pH-Responsive and Sustained Release Hydrogel Systems

The pH-responsive delivery systems especially apply to the soil-based application where space and time variations in pH

contribute to the availability of nutrients and root activity. The pH responsive hydrogels offer the controlled and sustained delivery of the nutrients and bioactive factors that are encapsulated. The recent advancement in PH responsive nitrogen fertilizer hydrogels has already shown long release characteristics in an irrigated soil environment leading to better nutrient use efficiency and less nitrogen loss to the surrounding environment<sup>34</sup>.

In addition to their release-regulating role, the hydrogel-based systems enhance the soil water retention and the availability of moisture, which is highly important under the conditions of drought. Multifunctional properties allow hydrogels to be used as both delivery systems and conditioners of the soil to

maintain the constant presence of preventative stress-reducing bioactive reagents and to increase the resistance of plants to abiotic stress.

### 6.3 Foliar Uptake and Systemic Translocation Pathways

Foliar delivery is fast and effective as a method of plant delivery of bioactive agents especially when plants are in critical growth or the case of acute stress. Formulations constructed using nanoparticles when applied to the surface of the leaves can reach the plant tissues either via stomata or cuticles. Foliar nanoparticle applications have been studied in detail to give mechanistic understanding of absorption, internal transport and physiological interactions in plant systems<sup>35</sup>.

After absorption, nanoparticles may overcome xylem and phloem tissues, allowing bioactive agents in encapsulations to be distributed throughout the body. This specific motion increases the efficiency of delivery and the overall amount of active compounds that is needed is minimized. The foliar uptake and translocation can only be understood mechanistically to design delivery systems that are optimal on bioavailability and minimum environmental exposure and non-target impacts.

### 6.4 Targeted Delivery via Biorecognition-Based Strategies

The most precise methods of managing agricultural inputs are targeted delivery systems. Nano-carrier systems can be designed to attach to a target cell or tissue or intracellular compartment by integrating bio-recognition motifs onto nanocarrier platforms, which allows the delivery system to selectively bind to a particular cell or tissue or intracellular site in a plant. With the help of such strategies, one can perform targeted transport and local discharge of chemical cargo at the plant level to provide high specificity of delivery and functional efficiency<sup>36</sup>.

Targeting Biorecognition Biorecognition reduces nonspecific interaction and off-target accumulation which improves agronomic performance and biosafety. This method is especially useful in the case of stress-reducing bioactive agents with low concentration and localization necessary to activate signaling pathways. Targeted delivery is thus a very important move towards next-generation precision agriculture.

All in all, the controlled release and targeted delivery systems have decisive functional benefits to the use of stress-reducing bioactive agents. These systems are characterized by stimulus responsiveness, sustained release behavior, effective foliar transport and targeting of molecules which make them greatly better delivery precision and minimizing environmental hazards. Further optimization in the future will be critical in creating resilient, resource-efficient and sustainable agricultural systems with mounting stress on climate.

## 7. Impacts on Crop Tolerance and Agricultural Sustainability

The achievement of stress-reducing bioactive agents and novel delivery mechanisms need to be ultimately determined by their effects on crop tolerance, crop productivity, and environmental sustainability. Stressfully, there is growing meta-analytical and large-scale evidence to support the claim that biologically determined inputs and controlled-release technologies can play major roles in increasing the performance of crops in stressful environments and decreasing the negative externalities on the environment. This kind of evidence is essential to support the practical importance of innovations in formulation and delivery to the practical use of agricultural systems.

### 7.1 Enhancement of Crop Stress Tolerance

The use of plant growth-promoting rhizobacteria (PGPR) has been widely known to be effective biological agents to improve crop resistance to drought stress. Combined field and controlled-environment studies show that the application of PPRG can be used to enhance the growth and physiological functioning of plants in a water-limited environment by significant amounts<sup>37</sup>. The positive effects are mainly due to the enhanced root growth, better nutrient uptake and the alteration of the stress-responsive signaling pathways.

The molecular mechanism behind the effects of PGPR on host plants is that it can modulate the expression of genes of drought-responsive functions of osmotic regulation, antioxidant defense, and hormonal signaling. Recent meta-analysis has found that the transcriptional reprogramming of drought cellular protection in relation to the action of PGPR is highly linked to promoting adaptability to stress among plants<sup>38</sup>. These findings can be used to highlight the significance of biological inputs in enhancing intrinsic stress tolerance systems instead of depending on external stress management.

### 7.2 Effects on Crop Productivity and Yield Stability

In addition to the tolerance of stress, there are undisputed advantages of integrating enhanced nutrient management strategies on crop productivity. Controlled-release fertilizers, especially controlled-release urea have been reported to drastically enhance crop yield by matching the availability of nitrogen with the demand of plants. Massive meta-analytical research shows that urea in controlled-release form promotes rice crop production but at the same time, minimizes nitrogen emission to the environment<sup>39</sup>.

On the same note, it has been reported that the combination of organic fertilizers with controlled-release urea enhances yield of wheat and efficiency in the use of nitrogen. These combined nutrient plans maximize nutrient supply during the growing period, culminating in more stable formation of yield and less prone to environmental stress<sup>40</sup>. The results identify the delivery technologies as a way of closing the divide between crop nutritional needs and effective fertilizer management.

### 7.3 Environmental Sustainability and Reduction of Nutrient Losses

The ability of the controlled-release and biologically based inputs to decrease environmental pollution is one of the greatest benefits. Nitrogen leaching is the other significant problem of traditional fertilization systems which lead to groundwater pollution and degradation of the host ecosystems. Four-decade of data of a global meta-analysis found out that nitrate leaching vulnerability differed substantially among different types of fertilizers, with controlled-release and organic amendments all being linked to less nitrogen loss than the traditional synthetic fertilizers<sup>41</sup>.

Meta-analyses that are supported by machine-learning also establish that controlled-release urea decreases reactive nitrogen losses without lowering or decreasing crop productivity. Such decreases in nutrient loss have a direct effect on the quality of water, reduced greenhouse gas emissions, and a subsequent long-term increase in the health of soils. These are essential to make agriculture more sustainable in the face of more climatic pressure. According to the findings of meta-analytical and large-scale research, Table 4 presents the impacts of the biological inputs and controlled-release nutrient strategies on crop stress tolerance, yield stability, nutrient and environmental sustainability.

**Table 4: Impacts on Crop Performance and Sustainability**

Category	Intervention	Main Impact	Sustainability Benefit	Key Evidence
Stress tolerance	PGPR	Enhanced drought tolerance and plant growth	Strengthens intrinsic plant stress responses	[37, 38]
Yield stability	Controlled-release urea	Increased and stabilized crop yields	Improved nitrogen use efficiency	[39]
Nutrient management	Organic fertilizer + CR urea	Improved yield and nutrient availability	Reduced fertilizer losses	[40]
Environmental impact	Controlled-release & organic inputs	Reduced nitrate leaching	Improved water quality	[41]

#### 7.4 Integrated Impacts on Agricultural Sustainability

The synergies between biological inputs and controlled-release technologies are demonstrated by the combined evidence and features of their complementary contribution to enhancing agricultural sustainability. Controlled-release fertilizers and others: improving the efficiency of nutrients and minimizing environmental losses, PGRs increase the stress-responses of plants in physiological and molecular contexts to improve their resilience. These combined strategies will lead to a more sound agroecosystem, which can stay productive even with abiotic stress and has the least ecological footprints. Notably, the meta-analytical data proves such strategies are most efficient during stresses, i.e., drought when the conventional inputs cannot be used to guarantee a stable benefit. Stress-specific activity highlights the importance of incorporating stress-receptive bioactive agents into complex delivery systems into climate adaptive agronomy.

In general, stress-reducing bioactive compound effects and controlled-delivery technology effects go beyond yield improvement to include more sustainability benefits. These methods offer a scientifically proven way of achieving resilient and sustainable agricultural systems by enhancing crop tolerability and stabilizing yields and production, as well as by limiting environmental pollution.

#### 8. Conclusion

The increasing complexity of climate induced stressful environments requires a fundamental change in the design, delivery and assessment of agricultural inputs. This review points out that the enhancement of crop resilience cannot be based on the augmentation in terms of the amount of inputs to be used, but the precision in the functions of these inputs, and their biological suitability. Hormones, protective metabolites as well as microbial and seaweed-derived bio stimulants are numerous examples of stress-reducing bioactive agents with a potent potential of supporting endogenous plant defense and adaptive processes. Nevertheless, the complete agronomic prospect is achieved when they are paired with formulation and delivery systems that support bioactive availability by aligning bioactive availability to plant physiological demand and environmental dynamics. The use of sophisticated formulation efforts using biodegradable polymers, nano- and micro architected carriers, and hydrogel matrices prove that delivery is not just a matter of technology, but a defining determinant of biological activity as well as sustainability. Regulated and focused release systems allow the perception of stress and bioaction to be synchronized, minimizing losses, minimizing off-target effect, and enhancing the resource-use efficiency. Notably, findings of meta-analyses emphasize that these innovations can be most effective at times when an environment gets stressed and conventional inputs are likely to fail, indicating their importance in terms of the strategy of climate-adaptive agriculture. Moving forward, biological inputs and intelligent delivery system integration not only creates a new opportunity of precise stress management, but also introduces some critical challenges.

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