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Synthetic and Natural Phytohormones: A Review and Analysis of their Development, Functions, and Impacts

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Abstract

Plant hormones are compounds synthesized naturally by plants, which regulate growth and development. In this paper, we survey recent developments in understanding the complex roles of eight small molecule plant hormone classes–abscisic acid (ABA), auxins, brassinosteroids,cytokinins, gibberellins, jasmonates, salicylic acid, and strigolactones–of which we primarily focus on cytokinins and auxins regarding their natural and synthetic versions. We then analyze the environmental and societal impacts of commercial usage of these hormones' on an industrial scale. While plant hormones have potential in stimulating antioxidant production in certain plants and stem cell growth, excessive plant hormone usage in the agricultural sphere can have negative consequences which must be considered prior to application.

Keywords: Plant hormones, Phytohormones, Auxins, Cytokinins

1. Introduction

Phytohormones are shown to regulate various functions of plants, including cell differentiation and division, organ formation, seed dormancy and germination, and senescence, while monitoring external activity and its effect on plant stress (Dobrev, 2005). These compounds are vital in maintaining essential systems within the plant, such as opening and closing the stomata and boosting immunity against stressors and pathogens. Plant hormones have been studied as potential avenues for research in promoting the biosynthesis of therapeutically-relevant compounds, as well as promoting antioxidant properties of specific plants to fight a variety of illnesses.

Additionally, synthetic plant hormones mimic their natural counterparts' structure and function and are frequently used in the agricultural industry to improve plant growth dynamics and crop yield, both of which are beneficial to combating global population growth. Due to these abilities, plant hormones, and the potential social and environmental consequences of their application, have become a significant area of interest for scientists and

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agriculturalists alike. Learning to utilize synthetic hormones efficiently to our advantage is crucial in such industries as specific amounts of hormones, when applied to plants, can effectively enhance reproduction rates. This paper explores both natural and synthetic hormones and their wide-spread use in commercial agriculture and beyond.

2. Overview

Each class of plant hormones is produced uniquely within specific plant regions and helps maintain all aspects of growth and development, ranging from pathogen defense to stress tolerance and reproductive development. For example, indole-3-aceticacid (IAA), a natural auxin synthesized from tryptophan primarily in the plants' leaf primordia and developing seeds, is later be transported to the vascular cambium and procambial stand, where it produces a growth response (Davies, 2010). On the other hand, cytokinins are biosynthesized in root tips and prevalent in plant tissue. From there, the hormones are concentrated in areas of heightened cell division, such as the subapical root zone, where it can stimulate cell division, differentiation of axillary buds,and regulate shoot growth.

Table 1. The physiological effects and biological targets of each specific plant hormone group: abscisic acid, auxins, brassinosteroids, cytokinins, gibberellins, jasmonates, salicylic acid, and strigolactones.

	Physiological Effects	**Biological Targets**
Abscisic Acid(ABA)	Promote senescence and stress responses in abscising organs, seed desiccation tolerance (Finkelstein,2002; Finkelstein, 2013; Sah, 2016)	1. ChIH/ABAR: seed development and stomatal movement 2. GTG1/GTG2: stomatal opening and closing (Guo, 2011)
Auxins	Apical dominance, phototropism, gravitropism, vascular tissue differentiation, delays ripening(Palmiye, 1970; Abel, 2020)	1. AFB2, AFB4, AFB5: seedling development 2. TIR1 and AFB2: encourage auxin signaling (Prigge, 2016)
Brassino-steroids	Germination, senescence, responses to biotic and abiotic stressors (Yang,2015)	1. BRL1: cell development, extreme temperature tolerance (Caño-Delgado, 2004) 2. BRL2: targeted protein degradation,vesicle trafficking, signal transduction (Ceserani, 2009) 3. BRL3: drought tolerance (Fàbregas,2018)
Cytokinins	Release of apical dominance, delay senescence, chloroplast development(Amasino, 2005; Palmiye, 1970)	1. CRE1/AHK4, ZmHK1: promote signals transmission (Lomin, 2012)
Gibberellins	Flowering, enzyme production, implementation of maleness in dioecious plants (Gomi, 2003)	1. GID1: crucial in regulating transcription withi the GA-signaling network (Gomi, 2003)
Jasmonates	Respond to various abiotic and biotic factors, regulates the plants' immunity (defense) and development (Wasternack, 2002; Katsir, 2008)	1. MYC2/3/4 receptor: promote expression of catabolic enzyme genes (Zhu, 2015) 2. COI1 receptor: mediates signaling and degradation of JAZ repressor proteins (Katsir, 2008; Sheard, 2010)
Salicylic Acid	Thermogenesis, disease resistance (Klessig, 1994)	1. NPR1 receptor: direct Ref to gene activation 2. NPR3/NPR4 receptors: negative regulators of immunity (Kuai, 2015)
Strigolactones	Induce germination of parasitic weeds, inhibit shoot branching (Zwanenburg, 2015)	1. DWARF14 receptor: strigolactone detection and degradation (Yao, 2016; Seto, 2019)

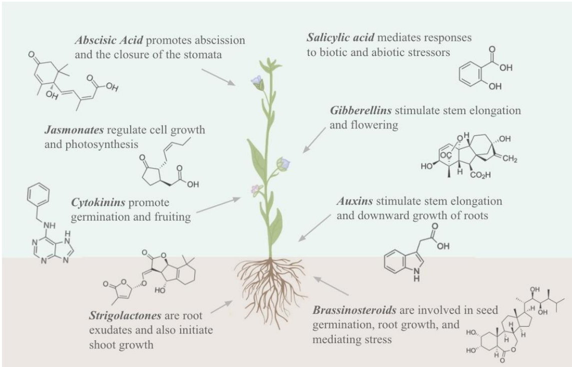

Figure 1: The locations at which the main classes of plant hormones are most commonly found in plants are illustrated above. In addition to others, these hormones occur in varying amounts depending on plant species and surrounding conditions, among many others.

3. Natural versus Synthetic

The foremost differences between natural cytokinins and synthetic cytokinins are exemplified in biological studies concerning their effects on plants' growth and development. Previous studies tested the variation between benzylaminopurine (BAP) and natural cytokinins found in *Moringa oleifera* extract (MLE), although both natural and synthetic hormones significantly helped produce more vegetative and flowering branches, natural cytokinins had more antioxidant activities, correlating with increased defense against stressors and nutrient quantity within plants (Anantharaj, 1970). The studies' findings indicate that while both synthetic and natural cytokinins help increase plant production, most natural phytohormones possess other functions that synthetic plant hormones are unable to mimic completely.

3.1 Structural and functional mimicry

Structural variations between natural and synthetic hormones result in differing interactions within plants. Due to their difference in structure, many synthetic and natural plant hormones will also differ in size, their polarity in the head group, the number of hydrophobic and hydrophilic chains the molecule has, as well as their saturation degrees. These subtle differences will result in different properties as well as in their fulfillment in biological activity (Flasiński, 2014). For instance, the auxin IAA can influence and interact with lipid monolayers more profoundly than that of 1-naphthaleneacetic acid (NAA), a synthetic auxin, due to the difference regarding aromatic ring size between the two hormones (Calderon-Villalobos, 2010). Similarly, all cytokinins have adenine and function in plant growth and development. Figures 2a and 2b highlight the structural similarities and differences between natural and synthetic auxins and cytokinins respectively.

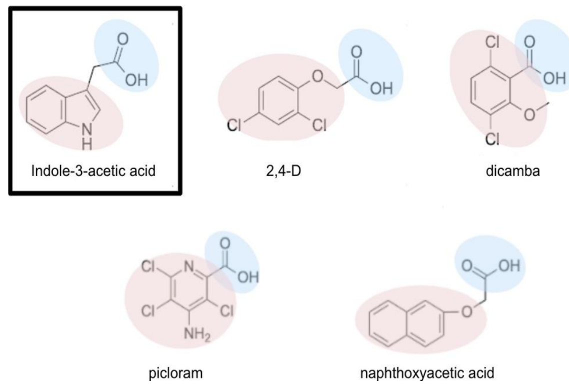

Figure 2a: Naturally occurring auxin, IAA, structurally compared to various synthetic auxins. Structural similarities are highlighted in blue, and structural differences are highlighted in red.

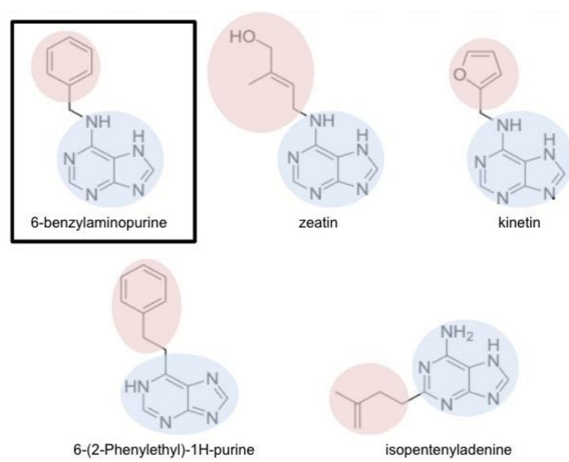

Figure 2b: Synthetic cytokinin, 6-benzylaminopurine, structurally compared to various naturally occurring cytokinins. Structural similarities are highlighted in blue, and structural differences are highlighted in red.

4. Structural Relationships

Most auxins contain similar features that help facilitate interactions with auxin receptors and are critical for auxin activities: an aromatic ring and a carboxylic acid group. In general, the binding affinity of auxins depends on the size of the aromatic ring and its hydrogen-bonding partner. For instance, one auxin receptor called ubiquitin protein ligase SCF(TIR1), or just the TIR1, is commonly bound to auxins by having the auxin's carboxyl interact with a negative charge on the bottom of the TIR1. However, due to the various ring sizes/structure of different auxins, the binding affinities differ. IAA, which contains ahydrogen-bonding group in the aromatic ring (NH group), can form a hydrogen bond with TIR1 carboxyl group, thus having a stronger binding affinity compared to those without a hydrogen-bonding group (Calderon-Villalobos, 2010). Unlike most hormones, auxins bind with the protein without needing to alter the shape of the receptor. This is due to the fact that the binding site of TIR1 is indifferent to the different aromatic sizes of the various auxins, thus easily taking in different analogs (Ma, 2018).

Another major binding interaction can be found in the IAA receptors: Aux/IAA and auxin response factor (ARF), both of which regulate auxin-induced gene expression. (Figure 3a) The two work closely together to regulate gene expression efficiently. Typical ARF proteins would have a C-terminal domain similar to the domains III and IV of the Aux/IAA, allowing the two to interact with each other (Reed, 2001).

An example of a protein binding with cytokinin can be found between the 17-kD protein acceptor, generally found in mungbeans (*Vigna Radiata*) and zeatin. (Figure 3b) In the past, most cytosolic proteins involved with protein modifications, mRNA degradation, metabolic processes, and cell death, were found to bind with cytokinins with low binding affinity. However, the discovery of the cytokinin-binding 17-kD protein *Vigna Radiata* Cytokinin-specific binding protein (Vr CSBP) with a high binding affinity, signal sequences, and transmembrane domain presented an exception. The group, including Vr CSBP, hasevolved to bind with small-molecule ligands such as plant hormones like zeatin.

The structure of Vr CSBP has // Their binding pockets are much larger than these small molecules, allowing other molecules to enter the binding cavity along with solvent, sealing off the site. For example, the zeatin binding site is located deep inside the large cavities between the beta-sheet and C-terminal helix alpha 3, where Vr CSBP and other proteins bind to and later seal off with two compact water molecules (Pasternak, 2006).

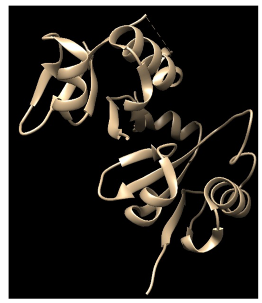

Figure 3a: 6L5K (ARF5 Aux/IAA17 Complex)

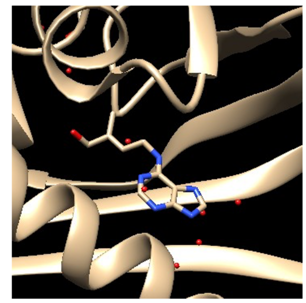

Figure 3b. 2FLH (Crystal Structure of cytokinin -speci binding protein from mung bean in complex with cytokinin)

Obtaining the crystal structures of the auxin and cytokinin complex's from the Protein Data Bank (PDB), and utilizing UCSF Chimera to view the structures, Figures 3a and 3b show the crystal structure of the auxin or cytokinin specific binding proteins respectively.

5. Impacts

5.1 Environmental Impacts

Plant hormones are primarily studied and utilized to improve agricultural yield on a large, commercial scale. By using synthetic phytohormones, crops can withstand disease more effectively and grow healthier efficiently, which is critical in sustaining the increasing agricultural demand due to the growing human population. From a controlled administration of plant hormones to plants' prolonged flowering, the hormones help result in overall growth as well as in a greater seasonal crop yield on a global scale (Raza, 2019). They can also be utilized to repair ecosystems after a drought (Basu, 2016). Plant hormones such as cytokines, which promote cell growth, can help alleviate water stress on plants (Othman, 2016).

Additionally, since each plant species is naturally accustomed to varying quantities and types of phytohormones, one species may be more receptive to large quantities of phytohormones while others may have inhibited function, such as stomatal closure, bud and seed dormancy, and stunted stem growth (Plant Hormones). This can foster deleterious mutations and could potentially harm both the plant and the ecosystem (Adamse, 1988; Batt, 2005).

Aside from environmental effects, other pressing problems regarding food chain impacts remain with phytohormones being utilized on a mass scale, such as their negative side effects on humans and other organisms. One study highlights how the regenerative properties of auxins might not have been favored through evolution due to a potential risk of cancer as a result of increased cell proliferation (Cernaro). These negative side effects on humans and the environment deter the use of phytohormones as growth stimulators in the agricultural industry.

5.2. Health Impacts

Despite potential environmental concerns, plant hormones have the potential to greatly benefit society, both pharmaceutically and commercially. For instance, cytokinin ribosides have recently been studied for potential usage as anti-cancer agents. They are known to inhibit growth and cause apoptosis in numerous cell lines, exhibiting activity that counteracts cancer, such as anti-angiogenic activity and the ability to stimulate immune responses (C. Amiable, 1970; Voller, 2010). Many other such applications of plant hormones exist in the pharmaceutical industry. By studying the role of various plant hormones within plants in regulating cell development, scientists have been able to translate many such ideas into the field of medicinal chemistry, which continues to be a growing area of interest in phytohormone research.

5.3. Social Impacts

Commercially, auxins can be utilized in plant nurseries to increase crop production through the formation of adventitious roots and synchronized initiation of senescence among flowers and fruits in crops. On the other hand, cytokinins may be utilized to deter pests and pathogens due to their disease-fighting abilities (Albrecht, 2017). This not only results in a higher crop yield but also improves the quality of crops produced in terms of food security. Pests are known not only to stunt crop growth but are also oftentimes harmful to humans when consumed. By reducing pests and the need to use toxic pesticides, both cytokinins and auxins provide a safer alternative to improve food security when harnessed correctly (Agrawal, 1998). Continuing studies with such phytohormones provide scientists and agriculturalists with new ideas surrounding developments in commercial agriculture and tackling these issues in particularly low-income regions. In these communities, food insecurity causes many people to struggle with chronic illnesses as a result of horrific management of nutritional needs, pest control, and toxicity measurements in foods (Seligman, 2010). It is especially crucial in these areas to have a better understanding of plant hormones and their properties to put an end to the cycle of lives being claimed by diseases associated with poor nutrition.

Phytohormones also promote microalgae production, which is beneficial in biotechnological applications. Found to enhance production, metabolite contents, and lipid aggregation, certain hormones partake in metabolic mechanisms and cell cycle regulation, further promoting metabolite and biomass production. They foster more resilient microalgae able to withstand abiotic stress in their local environments (Stirk, 2020).

6. Conclusion

Plant hormones have been found to have significant effects on several aspects of plant development, including stem and leaf growth, increased germination rates, and cell differentiation. Major plant hormones – auxins and cytokinins – have especially been studied using numerous biological assays, computational analyses, and pharmaceutical testing. Despite their seemingly beneficial nature, these phytohormones also have detrimental effects on the environment and beyond when synthesized for commercial use. These damaging effects can be examined by understanding the functions and primary usage of synthetically produced hormones versus their naturally occurring counterparts. As plant hormones continue to be utilized in agriculture and medicine, scientists and agriculturalists alike should be mindful of these environmental drawbacks and utilize these hormones both effectively and ethically.

Although their excessive use for industrial production poses many threats, the future of plant hormones is one with much potential. Due to their abilities to promote cell growth, plant hormones have been considered as possible avenues for research in promoting the biosynthesis of therapeutically-relevant compounds (Giannakoula, 2012; Bhullar, 2013). Other applications in the medical field include harnessing plant hormones for modifying stem cell production and enhancing the potential antioxidant properties of certain plants to fight various illnesses.

As the field of plant hormones becomes an increasingly prevalent topic in agricultural and scientific endeavors, it is important to consider both the benefits and possible detrimental effects of plant hormone usage. Despite these seemingly large challenges,the future of phytohormones is one with many applications, from agriculture to medicine.

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