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Elicitors: bioethical implications for agriculture and human health

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Abstract

In recent decades, agrochemicals have been used in agriculture to increase crop yields and quality and avoid losses due to pests. However, the use of these substances often imply environmental contamination and potential health risks. To move towards a more sustainable agriculture with less undesirable effects to human health, a novel line of research has recently emerged, proposing alternatives for the use of agrochemicals, such as elicitors. Elicitors, either biotic or abiotic, can stimulate plants biochemical mechanism to produce compounds that will result in desired agronomic traits, such as secondary metabolites to be used as nutraceuticals. This article shows the scientific and the ethic perspective of research projects evaluating the role of different elicitors in replacing the use of agrochemicals.

Keywords: Agrochemicals. Health. Biotechnology. Sustainable agriculture.

Resumo

Elicitores: implicações bioéticas para a agricultura e a saúde humana

Nas últimas décadas, compostos agroquímicos têm sido utilizados na agricultura para evitar pragas, nutrir o solo e aumentar a produtividade e a qualidade das plantas. No entanto, o uso dessas substâncias muitas vezes contamina o meio ambiente e traz riscos à saúde. Por isso, novas alternativas, como os elicitores, surgiram na produção alimentar a fim de consolidar uma agricultura mais sustentável, sem efeitos adversos para a saúde do consumidor. Os elicitores podem estimular o próprio metabolismo das plantas para produzir compostos que resultarão em características agronômicas desejadas, como metabólitos secundários para uso nutracêutico. Este artigo mostra a perspectiva científica e ética de projetos de pesquisa em que diferentes elicitores substituem agroquímicos.

Palavras-chave: Agroquímicos. Saúde. Biotecnologia. Agricultura sustentável.

Resumen

Elicitores: implicaciones bioéticas para la agricultura y la salud humana

Los compuestos agroquímicos se han utilizado en la agricultura en las últimas décadas para evitar pérdidas por plagas, nutrir la tierra, aumentar el rendimiento y la calidad de los cultivos. Sin embargo, el uso de estas sustancias en muchas ocasiones representa una fuente de contaminación ambiental y riesgos a la salud. Por ello, han surgido nuevas alternativas en la producción alimentaria, como el uso de elicitores, para consolidar una agricultura más sostenible y sin efectos adversos a la salud del consumidor. Los elicitores pueden estimular el metabolismo propio de las plantas para producir compuestos que resultarán en rasgos agronómicos deseados, como metabolitos secundarios de uso nutracéutico. En el presente artículo se muestra la perspectiva científica y ética de proyectos de investigación en los cuales se emplean diferentes elicitores para sustituir el uso de agroquímicos.

Palabras clave: Agroquímicos. Salud. Biotecnología. Agricultura sostenible.

Update

The authors declare no conflict of interest.

Agriculture has been one of the main pillars of society since ancient times, being transformed according to human needs. Since 1960, with the Green Revolution, one of the major strategies to improve agricultural productivity was the introduction of agrochemicals such as pesticides, insecticides, herbicides, and fertilizers [1]. Besides improving productivity, they also increased farm profitability, reduced labor, lowered fossil fuel consumption, increased crop yields, reduced food costs, and improved product quality [2]. Nevertheless, crop yields declined or even stagnated in developing regions [2], with the number of undernourished people worldwide amounting to 925 million in 2010, 98% of whom from developing countries [3].

Despite their advantages, agrochemicals are controversial due to their negative environmental impacts [1]. Pesticide overuse leads to pest resistance and harms beneficial insects present in the environment [3] and their penetration within the subsoil and aquifers poses risks to the environment and human health [4]. Agrochemicals also have a high carcinogenic and teratogenic effect. High doses and long-term exposure to organophosphorus compounds interfere with hormone regulation [3] and are associated with various undiagnosed chronic noncommunicable diseases, affecting the cardiovascular, hepatic, renal, nervous, and reproductive systems, such as chronic kidney disease of uncertain etiology and leaky gut syndrome – common disorders in several Central American countries, parts of Mesoamerica, southern Europe, India, and China [4,5].

The lack of legislation on the management of agrochemicals cause developing and least-developed countries to handle these substances indiscriminately and to apply chemical regulations only on export products [6]. In turn, more than 500 agrochemicals were banned from developed countries such as those from the European Union (EU) and the United States due to their harmful effects [7].

In the EU, the compliance with the permissible limits of pesticides established in the food legislation is verified by the European Food Safety Authority (EFSA), based on EU Regulation 396/2005 [8]. As for the US, the Environmental Protection Agency (EPA) evaluates the potential impacts of different agrochemicals on both the environment and human health, besides reviewing and verifying security measures and the compliance with regulations according to the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and the Federal Food, Drug, and Cosmetic Act (FDA) [9-12].

From the biotechnology perspective, the line of research aiming to develop alternative products and treatments for the use of agrochemicals integrates several fields of knowledge, such as chemistry, biology and engineering. This lead the definition of biotechnology to acquire different meanings throughout the last century [13]. Yet, we understand plant biotechnology as the set of biological phenomena and factors involved in the improvement of agriculture, food, and other derived industries. As such, bioethics in agriculture must offer a promising solution to face challenges related to food demand by addressing ethical and sociocultural concerns to ensure widespread confidence and acceptance of both producers and consumers [14].

By 2050, food production is expected to double in response to the exorbitant population growth, which will increase the use of agrochemical compounds in the upcoming decades [1]. Such increase implies health risks to the population, thus demanding new biotechnological tools to reduce or replace these substances use. Among the various available approaches and/or strategies, elicitors are stress stimuli capable of triggering plants defense response and adaptive capacity when applied in small amounts through the production of secondary metabolites, known for their nutraceutical role in feeding. As plants are constantly exposed to stress conditions, they have developed tolerance strategies to cope with adverse environments and suffer minimal morphological alterations [15,16].

Stress factors can be categorized as biotic or abiotic depending on their source and impact on plants. Whereas eustressor is a positive stimulus, capable of inducing plants immune response, distress is a stimulus with negative effects on the plant, such as death [17]. In this sense, every stressor is considered an elicitor, being classified in the same way as stress stimulus factors, into biotic or abiotic.

Biotic elicitors are substances produced by living organisms, such as proteins, carbohydrates, bacteria, fungi, and phytohormones (plant hormones). Several studies have approached phytohormones due to their interaction with various physiological and metabolic responses in plants [18]. They have also been referred to as biostimulants, given the great diversity of compounds with a specific biological function [19].

In turn, abiotic elicitors are physical stimuli to which plants are susceptible, such as light, temperature, long-distance electrical signals, electromagnetic waves, radiofrequency waves, and perception and response to mechanical stimuli and acoustic emissions [20,21]. As a result of associative learning to adapt to different environmental conditions, plants have developed extensive engineering signaling [22]. Therefore, elicitors activate signals that enhance secondary metabolites production, triggering plant defense response [18].

Provided these elements become effective biotechnological tools, the potential interest of industrial sectors in commercializing scientific breakthroughs as products or technological packages is one of the concerns regarding elicitors use. With the development of genetic engineering, the patent system was extended to include biology and biotechnology, sparking an important discussion given that biotechnology patents pose specific problems when large biotechnology companies seek to obtain commercial benefits only [23].

However, the bioethical evaluation of studies approaching elicitors is limited to the academic sector, so that new alternatives seek to address the urgent need for methods based on biologically active, environmentally friendly, and safe substances. In that sense, biostimulants are factors that intervene in the natural processes of plant nutrition, possibly improving nutrient use efficiency, the abiotic stress tolerance mechanism, quality traits, and increasing nutrient availability [24].

As discussed above, the general purpose of elicitation is to interact with biochemical pathways to produce secondary metabolites. Regardless of the evidence available on this aspect, one cannot generalize these strategies effect, given that plant metabolism response depends not only on the study model, but also on the type, concentration, and duration of the stimuli used [25,26].

To ensure a rapid recognition of stress and the activation of defense responses, we must also learn what type and dose of stressors can induce an epigenetic response in the plant. These measures may be critical for the timely activation of the defense system and, consequently, for the physiological adaptation to stress [27].

Potential elicitors

Elicitors are sustainable agricultural alternatives to agrochemicals in the production of food and other products for human use. Different types of elicitor compounds have been employed in agriculture according to their mechanism of action, but all of them influence plant growth, development, and gene expression. But the concept of elicitors is relatively new and is still under investigation.

Considering the need to communicate new scientific discoveries, we will describe below biotic (salicylic acid and hydrogen peroxide) and abiotic (acoustic emissions and UV light) elicitors with potential application in the agriculture.

Acoustic emissions

Environmental sound acts as a signal mediator in the ecological and adaptive processes of plants. Studies have shown that acoustic emissions (AE) could be used as indicators of plants water stress in response to environmental changes. These findings sparked interest in the mechanisms involved in the detection and emission of acoustic vibrations, particularly under specific environmental conditions.

Plants present a frequency-selective sensitivity for they can grow and orient themselves towards a 200-300 Hertz (Hz) sound propagation source [28]. They also have specific sensory mechanisms for detecting frequencies; those emitted by insects (500 to 2,000 Hz), for example, increase plants glucosinolate content [29].

Although still under discussion, studies have proposed that elicitation with AE may induce

several response mechanisms, such as improved drought tolerance [30] and the production of bioactive compounds with antioxidant activity, such as carotenoids, phenols, and bioactive peptides [31]. AE use in agriculture aims to intensify the absorption of substances or nutrients that will reduce chemical applications and production costs, thus representing an environmentally-friendly alternative for agricultural production [32].

Ultraviolet light

Ultraviolet radiation (UVR) is a type of solar radiation covering the wavelength range of 100-400 nm, divided into three bands: UV-C (<280nm), absorbed by the atmosphere; UV-B (280-315nm), which arrives partially; and UV-A (315-400nm), most transmitted to the Earth [33]. About 7% to 9% of the total solar radiation reaching the biosphere corresponds to UVR; it is a highly energetic radiation [34] that provokes reactions in the molecules affected by it. These reactions are often associated with sunburn and skin cancer, so that the general conception of UVR is negative [33].

Although possibly harmful to humans, UVR plays a vital role in providing plants with the necessary energy for photosynthesis and growth from germination to flowering. Among plants defense mechanisms, we may find the photorepair processes and their antioxidant capacity, which protect them against UV and other stressors [35]. This indicates that plants evolved to perceive the presence of UVR and exploit it efficiently without damaging their biomolecules.

In fact, UV-B radiation has been reported to enhance plant survival under biotic and abiotic stress conditions. For example, low doses of UV-B can induce plants defense responses to photo-oxidative stress and pathogen infections such as those caused by the fungus *B. cinerea*, improve heat tolerance, and provide protection at freezing temperatures under laboratory or field conditions [36]. Thus, the use of UV light to optimize crop productivity and quality is gaining increased interest due to its properties of altering secondary metabolism and positively regulating plants antioxidant response [37].

Salicylic acid

Salicylic acid (SA) is a phenolic compound synthesized by plants. For playing a key role in regulating plant growth and development, it is considered a phytohormone [38]. SA spray application has several effects on plants, such as boosted flower production and high efficacy against fungal attack [39]. During pathogen attack, this compound rapidly accumulates at the infection site and spreads to different plant parts to induce systemic acquired resistance [38].

Many are the examples of physical and synthetic elicitors being successfully used as immunostimulants in agriculture, especially those whose defense-inducing capacity is sufficiently potent to substitute conventional agrochemicals [40]. Most synthetic elicitors capable of triggering plants defense responses belong to the large group of SA analogs, with the ability to protect crops from diseases without necessarily being toxic to pathogenic organisms [40].

SA is also involved in several physiological and biochemical processes such as photosynthesis, osmotic balance, secondary metabolites production, induction of the antioxidant defense system, and expression of genes involved in defense response against a wide range of biotic and abiotic stresses [41].

Hydrogen peroxide

Hydrogen peroxide (H_2O_2) is a compound generated during aerobic metabolism that belongs to the reactive oxygen species (ROS). Although considered harmful due to its oxidative activity, H_2O_2 functions as a signaling molecule in the control of plant physiology [42] and therefore can increase growth parameters and improve plant anatomy [43].

By being one of the first compounds produced in response to different types of stimuli and participating in tolerance mechanisms, H_2O_2 also plays a key role in stress response mechanisms. This compound is responsible for activating several regulatory pathways, as calcium-dependent signaling, protective molecules biosynthesis, and phytohormone-associated pathways such as SA and abscisic acid, besides triggering some MAP-kinase cascades and the synthesis and regulation of ROS pathway [42,44].

This triggering converge into the synthesis of transcription factors and gene regulation by, for example, activating the expression of genes that can induce resistance response to environmental stress conditions [42].

To mention some examples, H_2O_2 has a positive effect on tolerance to salt stress [45], drought, waterlogging [46], high temperatures, and low light conditions. Similarly, the exogenous application of hydrogen peroxide can induce plants tolerance to virus infection and other pathogens [47].

Ethical discussion

Scientific knowledge about elicitors indicates that they are a viable option for addressing the challenges faced in agriculture. However, knowledge tends to be valued according to its usefulness to humans, so that various technologies implemented in society incurred adverse effects. Agrochemicals penetration within the soil and groundwater has affected both human and environmental health, so that we will discuss these elicitors application from the ethical principles, considering their impact on society.

Understanding how elicitors induce secondary metabolite biosynthesis requires an in-depth study of the complex defense-signaling pathways and networks of plants. Each type of elicitation, be it chemical or physical, causes different impacts on plant stress physiology. In that sense, advancing knowledge on these elicitors means to advance knowledge on plant immunity [40,48], which requires both science and technology to shoulder ethical responsibility, being relevant and easily transferable to people of different cultural and social backgrounds.

Principle of beneficence

The use of elicitors confer a wide range of direct benefits for agricultural productivity, reducing damage caused by fungi, pests, insects, herbivores, and some pathogens [41], as well as those caused by environmental factors [49]. Elicitation processes may be applied through different methods, but the most common is spraying. Elicitors such as SA and H_2O_2 can be easily applied to different cropping systems by spraying [49], and physical elicitors such as AE and UVR are easily combined with other chemical or biological treatments [50].

Elicitor-induced stress often leads to the accumulation of bioactive compounds used as nutraceuticals in humans, thus having a positive impact on health. Moreover, the mechanism of action of elicitors and plants immunity activators is directed to the innate defense system in the plant-host interaction, so that their use presents no risk of selecting agrochemical-resistant pathogen strains such as fungicides, insecticides, and herbicides – one of the major threats to global health and food security [51].

Principle of non-maleficence

To date, no evidence has been found on the collateral damage of biotic or abiotic elicitors to plants, humans, or the environment [39,41]. In fact, elicitor treatments could be an alternative to genetically modified plants, bearing lower ecological risks [49].

Plants elicitation is hardly likely to harm humans due to its application techniques. For requiring specialized equipment such as horns, amplifiers, UV lamps, and photoselective coatings, abiotic elicitors as AE and UVR can only be applied to agricultural production in controlled environments. Likewise, manipulating greenhouse lighting is a common technique to optimize productivity that, when applied within controlled spaces, mitigates possible collateral risks to humans and other animals. Abiotic elicitation by UV-B or UV-C, for example, is unharmful for both humans and other organisms: it requires a significant but short-term energy supply, stimulating the plant without altering its physical or nutritional composition [50].

As for biotic elicitors, the doses applied in agriculture are too low to induce any alteration in the environment or in living organisms. Although a strong corrosive considered hazardous to health, H_2O_2 is not carcinogenic, and to cause effects such as irritation it must be used in considerably high concentrations – above 5%, with a median lethal dose (LD_{50}) of 376 mg/kg (oral) and 4.06 g/kg (skin). H_2O_2 is commonly used as an antiseptic at concentrations of 3%,

whereas its applicability as plant stimulator employs nanomolar concentrations, which are 10 to 100 times lower. Salicylic acid (SA) is yet another noncarcinogenic and low-risk biotic elicitor. In blood, SA is harmful at levels greater than 35 mg/dL and its LD50 is 891 mg/kg for oral ingestion and 10 g/kg for skin contact [2]. Although commonly used in topical skin treatments at concentrations around 1%, as a plant stimulator it is used at lower concentrations. Moreover, both H_2O_2 and SA have a rapid photochemical degradation, so their permanence in the environment is ephemeral.

Principle of justice

The use of these sustainable alternatives in agrifood industry is accessible to all. However, establishing an elicitation treatment still has limitations regarding the type of plant and its physiological and genetic mechanisms, as well as to environmental factors and their influence on plant growth [50]. This points to the need for advancing knowledge on the complexity of diverse phenomena and conditions entangled in the use of elicitors, regardless of patented technological packages and large companies manipulation.

Assessment procedures for chemical and phytosanitary products (such as those established by the EFSA) among other related legislations must be introduced in the field to ensure a safe and responsible use of elicitation treatments. That is, authorities must implement standards and techniques to certify that elicitors applications imply no secondary risks such as the presence of toxic residues or relevant impurities, thus representing no risks to the food chain, producers, or the environment.

Principle of respect for autonomy

From crop selection to the production system, the agricultural activity is an autonomous practice that involves the use of specific products and techniques. In that sense, farmers get to choose more environmentally-friendly production methods, such as the use of elicitors, whereas consumers are free to choose the products they want to consume according to their production method.

However, establishing elicitors application as a fully autonomous practice requires greater dissemination of information on alternative crop improvement technologies, with in-depth knowledge about their advantages, disadvantages, and limitations.

Principle of precaution

Although no adverse effects have been reported in the literature, we must understand the various types of stimuli and how they act on the crop defense mechanism in order to improve protection and management of sustainable crops. Acoustic emissions (AE) underlying mechanism is still not fully explained, and we need more information regarding the interaction between sound waves and the biological functions of UV perception mechanisms, their signaling pathways, as well as the regulation and metabolic pathways involved in the biological response [50]. Open-field studies addressing the long-term environmental effects of SA and H_2O_2 as biotic elicitors and their interaction with other organisms are also scarce.

The primary goal of sustainable agriculture is to optimize the health and productivity of communities interdependent of soil life, plants, animals, and diverse social groups [53] such as farmers, producers, processors, and final consumers. The emerging issues in plant protection points to an urgent need for developing more efficient, sustainable systems and ecological tools, whereby the availability of innovative applications and molecular techniques opens up new possibilities for organic and sustainable agriculture. In that line, research have developed new strategies to directly protect plants against pathogens, possibly increasing immunity against their strains [53].

Principle of social responsibility

To address the staggered growth of the world population, food production must increase concurrently based on sustainable agrifood systems, requiring the use of products that improve agricultural productivity. In this scenario, elicitors offer a promising alternative for the use of agrochemicals, allowing us to meet such

requirements in a less environmentally damaging way. Moreover, elicitation treatments represent no danger for the natural resources that future generations will depend upon.

Many are the efforts to improve the prospects in the agricultural community and in society as a whole by offering alternative methods for the use of substitute chemical inputs. However, biostimulants, elicitors, and semiochemicals should not be used as exclusive agroecological management practices, but rather integrated into fertilization, disease, and pest control strategies to complement chemical inputs and help reduce their doses, application and frequency.

Final considerations

The use of elicitation treatments have been widely endorsed for their advantages; however, farmers and growers are still quite unsure about employing elicitors on a massive scale, mainly due to their fluctuating field performance. Although highly interesting for crop protection and pest management, the development of techniques for elicitor-induced plant defenses is still in the early stages to reach large-scale agricultural use. In that sense, not only do farmers need more information on how to apply these tools in their field practices, but regulatory agencies, investors, producers, and consumers also need to be well-aware of the advantages of these alternative methods and their potential to promote sustainable agriculture [54].

Despite their acknowledged benefits, further studies are required to understand the environmental factors affecting elicitors efficacy, particularly for extensive crops. From an ethical perspective, elicitors comply with the principle of beneficence, by comprising bioactive compounds beneficial to human health; with the principle of non-maleficence, for being unharmful to both humans and the environment; and with the principles of justice and autonomy, by being an open access and application option for crops.

Thus, elicitors are promising alternatives for agricultural application, which justifies their study and implementation by the scientific and agricultural community to provide further knowledge on possible interactions between these products and the plant environment. All of the above exposed enable us to envision the possible implications of the large-scale use of elicitors based on government policies that favor alternative and safe agricultural production systems.

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