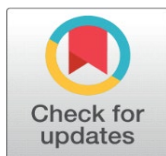


PHYTOCHEMICAL BIOPESTICIDES: RECENT DEVELOPMENTS AND MECHANISMS OF ACTION

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ABSTRACT

The concern over ecology and sustainable agricultural practices has led to increasing utilization of biopesticides. This chemical has proven itself to be a promising or worthy alternative to unsustainable/conventional chemicals, such as synthetic agrochemicals. These chemicals are extracted or derived from secondary metabolites belonging to plant species, offering actions that are precise, or “target specific”. It poses lower toxicity rates and provides greater scope for biodegradation, hence deeming away the perils of artificial chemicals, wherein non-degradable substances often cause hindrances in agricultural processes, like waste accumulation, rising infestation and so on. Previous research has highlighted the importance of understanding phytochemicals and the synergistic reactions they inhibit. This present study delves along similar lines to further shed light on agricultural processes that improves formulation stability and bioefficacy, with special emphasis on the utility of phytochemicals. We proceed to look at ongoing developments, mechanistic understandings and applications of our core topic, phytochemical biopesticides. We shall also be placing keen emphasis on extraction techniques, new-age technology, delivery systems and other commercial aspects of commercialization.

Keywords: Biopesticide, Phytochemistry, Agriculture, Sustainable Development, Ecology

1. INTRODUCTION

The prolonged use of synthetic chemicals have led to severe degradation of the environment. Pests have developed resistance towards these chemicals and it has gradually led to unproductive margins in the agricultural sector. Not to forget, these conventional methods or apparatus have led to adverse effects in both human and animal health. To address these pressing issues, experts have long favoured the use of phytochemical biopesticides. They primarily consist of alkaloids, phenolics, terpenoids and other essential oils, all of which collectively function as toxins or oviposition deterrents, specific to certain pests. It is worth noting that unlike conventionally used synthetic chemicals, phytochemical agents tend to display faster biodegradation rates and exhibit target specificity, thus deeming away the hindrances of waste accumulation. Understanding the interactive bond between

these chemicals and their target pests is vital, because the complexities of such physiological and biochemical proceedings unearth larger questions of incorporating or harnessing such chemicals for large-scale industries that are still faced with issues of sustainability and unhindered progress. Understanding the mechanism of action in phytochemicals is essential, mainly to understand their synergistic nature, and to grasp their ecological, as well as insecticidal potential.

2. MECHANISM OF ACTION

Studies have highlighted the disruption of neuroendocrine signaling in insects, as one of the core themes in phytochemical study. Specific kinds of alkaloids and terpenoids tend to mimic or simply antagonize endogenous insect hormones, ultimately leading to molting failures or developmental arrest. Let us have a brief look at a paradigmatic case, azadirachtin. It is a tetranortriterpenoid extracted from *Azadirachta indica* (neem), and is known for interfering in the neurohormonal regulation of ecdysis. These entities when introduced into agricultural systems or networks, tend to modulate the secretion of prothoracicotropic hormone (PTTH), and work through ecdysone biosynthesis, to drastically shorten the lifespan of pests/insects, by impeding the molting process and inducing morphogenic anomalies. Turning to the contemporary period, numerous studies have focused on how azadirachtin affects the midgut epithelial cell integrity, altogether reducing insect feeding behaviour through deterrent chemoreception pathways. The process also halts ovarian development, hence leading to systemic impacts across whole physiological systems. One other interesting category of phytochemicals, namely pyrethrins, which are basically derived from *Chrysanthemum cinerariifolium*, follows a neurotoxic method or plan of action. They enter insect neurons, acting on voltage-gated sodium channels, inducing repeated nerve firing, eventually leading to hyperexcitation, thus leading to paralysis or early death of the insect. It is also worth noting that previous electrophysiological investigations have shown that selective action shown by pyrethrins on insect but not mammalian sodium channels resides within the channel pore region and is attributed to amino acid residues differing subtly between the two channels, providing a basis for the selective toxicity of pyrethrins to non-target species.

Synthetic analogs including pyrethroids function in a similar way, however, they frequently lack the biodegradability of their botanical relatives. Additional-specific, nonlimiting examples of mitochondrial electron transport inhibitors include the rotenoids eg rotenone in *Derris* and *Lonchocarpus* species which inhibit electron transport of in mitochondrial at complex I such interference with are involved in oxidative phosphorylation and lead to ATP depletion and necrosis in insect cells. The mechanism of action of rotenone is well known, but new work has expanded our knowledge of their molecular targets using proteomic analyses, thus revealing that rotenoids may affect also other metabolic enzymes and cytoskeletal constituents, and therefore, it provides explanation for its multi-toxicity spectrum. These and other multi-target interactions have become known to be a characteristic feature of phytochemicals, in contrast to classical pesticides which tend to take effect on a limited number of targets only. Phytochemicals induce also a marked antifeedant and repellent activity, that is connected with the interaction of the compounds with the chemoreceptors of the insects and with the gustatory pathways. For example, molecules such as limonene and eugenol modulated TRP (transient receptor potential) channels and other chemoreceptors and induced rejection behaviors that compromise feeding and oviposition. Insects conditioned with these volatiles show changed locomotory patterns and lower levels of foraging,

a response corroborated now with neuroethological experiments that map the modulation of olfactory glomeruli due to phytochemicals. In addition, some phytochemicals act as feeding deterrents through anti-digestive enzymes. Flavonoids and tannins e.g., suppress amylase, protease and lipase in insect gut thus, affecting nutrient homeostasis which will lead to starvation in the long-run.

Advancements in molecular entomology have provided additional insights into these actions at the genetic level. Transcriptome analyses show that treatment with some phytochemicals leads to up-regulation of detoxification genes, including cytochrome P450 monooxygenases, glutathione S-transferases and carboxylesterases. Curiously, now we know that certain phytochemicals are actually inhibitors of the same enzymes increasing these natural toxins. Such biochemical antagonism forms the rationale of attenuating the same through combinatorial use of phytochemicals with synergists to improve their bioefficacy. Moreover, RNA interference (RNAi) technology has also recently revealed the relevant target genes acted on by phytochemicals, which will help to understand the role of phytochemicals as gene-regulatory agents towards the integrated pest management. The ecological dimension of phytochemical action is also increasingly interpreted in the context of evolutionary chemical ecology. CO-EVOLUTIONARY ARMS RACE: The continuous struggle between plants and herbivores has generated a variety of secondary compounds that are well tuned to take advantage of the weak points of the physiology of insect pests. This co-adaptation allows selective phytotoxicity of specific phytochemicals and is consistent with an increasing body of research demonstrating that pest resistance to phytochemical biopesticides appears to evolve more slowly than resistance to formulated synthetic preparations. In addition, synergistic effects between classes of phytochemicals (i.e., between alkaloids and phenolic compounds, and between terpenes and flavonoids) exist, which can result in combinatorial effects that increase toxicity or circumvent the defenses of pests. These interactions are being studied using a system's biology approach including metabolomic and network modelling for the ability to predict and manage cool synergisms for field use.

3. DEVELOPMENTS IN EXTRACTION AND FORMULATION

Both extraction and formulation of phytochemical bio-pesticides are important steps in their development pipeline, as they have strong impacts on the efficacy, stability, and commercialization of the products. In the past, the extraction of bioactive compounds from plant matrices used conventional processes, for example maceration, percolation, and soxhlet extraction, which although effective to some extent, suffered with inefficiencies including thermal degradation, solvent wastage, and yield of only limited quantity of thermolabile or volatile compounds. Recent decades have seen a drastic change in trends favoring better greener, efficient, and advanced extraction techniques due to the dictates of green chemistry issues with high selectivity and reproductivity towards the increasingly sustainably sounder earth espoused in the phytochemical industry. Among the most important innovations in this field we find the supercritical fluid extraction (SFE), especially with carbon dioxide as supercritical fluid. As a result of the tunable solvating power of supercritical CO₂ and its low toxicity and non-flammability, non-polar products, such as essential oils, terpenoids, and lipophilic alkaloids, can be specifically extracted at moderate temperature and pressure conditions. Some research reports have shown that the structural integrity of thermosensitive compounds are well kept and significantly lower co-extraction of undesired lipids and pigments are obtained with SFE than conventional extraction. This accuracy is justified in

principle by the application of phase equilibrium modeling and density-dependent solvation theory, which can be used to tailor pressure and temperature effect to particular molecular weight windows.

Adjuncts to SFE are microwave-assisted extraction (MAE) and ultrasound-assisted extraction (UAE,) both energy-saving methods incorporating physical phenomena in the disruption of the cell-wall and penetration by the solvent. MAE makes use of dielectric heating because when microwaves alter the polarity of molecules of polar solvents (such as water) or solutes present in these solvents, they are heated owing to molecular friction; such as this, they move inside the cells entering in contact with the food to be heated [7] and the water present in this food heats the food from inside. Dielectric theory pertaining to MAE implies that solvents that have high dielectric constants and dissipation factors would be more efficient which explains why aqueous ethanol and methanol are an ideal media for extraction of phenol and flavonoid. In contrast, UAE uses acoustic cavitation, in which high-frequency sound waves produce microbubbles that violently collapse to produce confined areas of high pressure and temperature. The diffusion of phytochemicals into the solvent medium is accelerated and mass transfer is improved by this mechanical effect. The classical cavitation and mass transfer models, which describe the connection between solute diffusivity, solvent viscosity, and ultrasonic intensity, serve as the theoretical foundation for UAE. Although there has been substantial progress in the extraction of bioactive components, creating phytochemical biopesticides presents unique difficulties. Many plant-derived compounds, particularly terpenoids and essential oils, are volatile, hydrophobic, and chemically unstable, which makes it difficult to use them in field settings. Advanced formulation technologies that improve these compounds' stability, bioavailability, and controlled release have been used in recent research to address this issue. In this regard, nanoformulation has become a game-changing strategy that uses nanotechnology to encapsulate phytochemicals in carriers that enhance their physicochemical characteristics. To improve the solubility, guard against UV degradation, and regulate the release kinetics of active compounds, nanoscale emulsions, liposomes, solid lipid nanoparticles, and polymeric nanocarriers have all been used. In contrast to traditional emulsions, essential oils encapsulated in chitosan-based nanoparticles have demonstrated increased persistence and adherence to leaf surfaces, as well as prolonged larvicidal activity against *Aedes aegypti*. Diffusion-controlled release kinetics and interfacial thermodynamics, which describe how nanoscale encapsulation lowers surface tension and permits gradual, targeted delivery, provide the theoretical underpinnings for these improvements. Hydrophilic and lipophilic phytochemicals can be encapsulated in liposomes or biodegradable polymeric matrices, such as those made from polylactic acid (PLA) or polycaprolactone (PCL), which offer biocompatible and biodegradable platforms. In order to rationally design formulations with optimal wetting, spreading, and adhesion properties, bio-interfacial theories and computational fluid dynamics are being used to model the interaction of these carriers with plant surfaces and pest physiology. Furthermore, the use of pH-sensitive or enzyme-responsive nanocarriers creates the potential for intelligent delivery systems in which particular circumstances in the insect's gut or on its cuticle surface cause the release of active ingredients. These systems are conceptually grounded in stimuli-responsive material science and have been experimentally validated in studies involving pests such as *Spodoptera litura* and *Helicoverpa armigera*. The idea of co-formulation, in which several phytochemicals or phytochemicals combined with microbial agents are formulated together to take advantage of synergistic interactions, has gained popularity in addition to individual formulations.

Through multi-targeted action, this strategy not only increases bioefficacy but also lessens the issue of resistance development. For example, formulations that combine neem oil with entomopathogenic fungi like *Metarhizium anisopliae* or *Bacillus thuringiensis* have demonstrated superior performance in terms of pest suppression. Pharmacodynamic synergy models and interaction coefficient analysis, which measure additive or synergistic interactions based on bioassay data, provide scientific justification for such co-formulations. Another area of focus is the stabilization of active compounds, particularly in field applications where environmental conditions can change. The effectiveness of phytochemical biopesticides can be jeopardized by oxidative degradation, temperature changes, and UV radiation. In order to combat this, formulation scientists have used antioxidants, UV-blocking agents, and microencapsulation techniques, which form protective barriers around the active ingredients. These systems' design is influenced by polymer physics and colloidal chemistry, specifically the theories of controlled permeability and particle surface modification. Last but not least, formulation developments need to be in line with socioeconomic, ecological, and regulatory contexts. Innovation in solvent-free formulations, biodegradable packaging, and easy-to-use application techniques has been spurred by the demand for organic and residue-free agricultural inputs. Additionally, compatibility with common spraying equipment, storage stability, and cost-effectiveness are necessary for the integration of these formulations into current pest management infrastructures. These issues are being addressed through interdisciplinary research that connects engineering, chemistry, and agronomy.

4. CONCLUSION

Phytochemicals exhibit remarkable biochemical diversity and multi-targeted functionality, starting with their mechanisms of action. Examples of naturally occurring secondary metabolites that disrupt insect neuroendocrine, respiratory, and digestive systems through highly specialized molecular interactions include rotenone, pyrethrins, and azadirachtin. These substances provide a biochemical redundancy that restricts the emergence of resistance because, in contrast to monofunctional synthetic pesticides, they work through integrated pathways, hormonal disruption, neural excitation, mitochondrial inhibition, and enzymatic suppression. In addition to being the result of intricate plant-insect co-evolutionary dynamics, this multifaceted efficacy is now better understood via the prism of contemporary molecular biology, which includes transcriptomics, proteomics, and receptor-target modeling. The practical constraints that previously prevented the scalability of phytochemical biopesticides have been addressed by recent developments in extraction and formulation technologies.

In keeping with the tenets of green chemistry, the use of green extraction techniques like supercritical CO₂ extraction, ultrasound-assisted extraction, and microwave-assisted extraction has greatly increased the yield, purity, and thermal integrity of active compounds while lowering solvent waste. Nanotechnology has created previously unheard-of opportunities for targeted delivery, controlled release, and stability improvement in formulation. In addition to increasing field efficacy, pH-sensitive polymers, liposomal carriers, and nanoemulsions are opening up precision agriculture applications. Phytochemical delivery becomes a scientifically rigorous field thanks to these formulation systems, which are based on well-established physicochemical theories such as mass transfer dynamics, colloidal stability, and interfacial thermodynamics. Crucially, this study also highlights the

increasing popularity of integrated pest management (IPM) techniques, which heavily rely on phytochemical biopesticides.

Their biodegradability, low effect on non-target species, and compatibility with microbial biocontrol agents all fit in nicely with the agroecological philosophy of IPM. Additionally, systems biology techniques and pharmacodynamic modeling are being used to design synergistic formulations that combine various classes of phytochemicals or phytochemicals with bioagents, illustrating the field's maturity and interdisciplinarity. However, difficulties still exist. Widespread adoption is still hampered by the lack of regulatory harmonization, stability in changing environmental conditions, and standardization of active ingredient content. Notwithstanding these obstacles, the industry is seeing a boom in investment and innovation due to recent changes in policy and rising consumer demand for food free of pesticides. Phytochemical-based biopesticides are currently being developed for commercial agricultural frameworks and national pest control programs, in addition to niche organic markets.

CONFLICT OF INTERESTS

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