REVIEW ARTICLE

Standardization, Quality Control, and Bio-Enhancement of Botanical Insecticides: a Review

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ABSTRACT

Botanicals are substances extracted from plants for use in various applications, such as the production of insecticides. Botanical insecticides (BIs) have recently attracted awareness in pest management owing to their potential to substitute synthetic pesticides. BIs are eco-friendly and more sustainable due to their ability to breakdown after use without generating toxic residues and diverse approach actions on targeted pests. Nevertheless, BIs are still not readily accepted, because the supporting proofs are very traditional, raising doubts about their quality. Additionally, the phytochemical variations of plants yield uneven and sometimes unfamiliar pesticide activity. This paper discusses challenges to overcome and presents the most noteworthy knowledge on BIs, their standardization, quality control, and bio-enhancement to be useful in agriculture and to improve human health.

Keywords: Botanical insecticides, pesticide activity, botanical standardization

1. Introduction

Globally, the 1.8 billion people who engage in agriculture utilize at some point at least one form of pesticide, from land nurturing to crop protection or management (Alavanja, 2009). The use of pesticides has expanded robustly from its inception in the nineteenth century to the twentieth century, along with agricultural productivity (Camara *et al.*, 2019; Mehrazar *et al.*, 2015). Unrestricted and excessive use of these chemicals has, however, substantially induced calamitous effects on human health (López *et al.*, 2005; Sucharita, 2014), environment (Shy, 1985), and non-targeted organisms (such as animals, fish, and plants) (Okwute, 2012). These studies have highlighted the need to develop and use alternative measures for sustainable crop protection and pest management. Therefore, this means swinging the pendulum of pesticides back toward the most eco-safe substitutes, which is the group termed botanical insecticides (BIs) (Isman, 2015). BIs represent a class of organic bio-pesticides derived from plant-based protectants and compounds such as pheromones, which have the capacity to manage plant infections and insects (e.g., the phytophagous bug) that have public health significance (Isman, 2020). Other include microbial biopesticides that target microbial infections in plants. Broadly, the BIs are classified into insecticides, herbicides, fungicides, molluscicides, nematicides, and rodenticides (Ortiz-Hernández *et al*., 2013). BIs are considered eco-friendly and sustainable for use owing to their ability to breakdown after use, not leaving behind any toxic residues and performing multifarious actions on marked pests (Hikal *et al*., 2017). For years, bioactive compounds such as pheromones extracted from plants were used by humans to control or manage pests and diseases before the advent of synthetic insecticides. BIs were used in ancient China, Greece, India, and Egypt to manage agricultural pests for over two millennia (Isman, 2006). Historically, scores of plants have been investigated and utilized over the years. Heal *et al*. (1950) described about 2,500 plants belonging to 247 families, used as BIs, all having toxic impacts on various insect species. Purohit *et al*. (2004) reported on 2,121 plant orders used as BIs. Since Dodia *et al*. opined that gathering information exclusively on plant classification is insufficient, the authors appraised and verified some plants for their potential as insecticides. They also noted that it is essential to analyze the human health and environmental risks of plant-based pesticides prior to usage. They found that over 120 species of plants were highly harmful to humans (Dodia *et al*., 2010).

Recently, there has been extensive search and analysis on finding alternatives to synthetic pesticides. Accordingly, different plants with eco-friendly bioactive ingredients that show proof of wide insecticidal upshot with negligible environmental and health damage have been used to develope insecticides. These results highlight the success of tests and utilization of natural products adopted by considering long-established data, i.e., the exploitation of classical literature and traditional knowledge on cultural folk practices, which are common among farmers (Sharma *et al*., 2010). However, BIs still face the challenge of unacceptability from growers, standard organizations, governments, and other agricultural stakeholders (Luiz de Oliveira *et al*., 2018). Firstly, this is because the supporting proofs for their usage are traditional, which raises doubts about quality. Secondly, the variation in the phytochemicals of plants leads to irregular and sometimes unfamiliar pesticide activity even among similar products that originate from a different region (Isman, 2015, 2020).

Chemical standardization of the bioactive component(s) is imperative prior to and during production to surmount these hurdles. Hence, the putative active ingredients of BIs require standardization along with strict quality control to guarantee unswerving composition, potency, and safety. Nevertheless, recent trends in the general acceptance of BIs as the best alternative to synthetic pesticides and their utilization remains low worldwide. This is generally ascribed to commonly reported issues revolving around uneven pesticide activities, classic literature data that requires re-evaluation, and governmental policies that insist on standardization. Considering all the above facts and parameters, this paper aims to present a critical overview of the most important knowledge about BIs, their standardization, quality control, and bio-enhancement to improve their use in agriculture and to protect human health.

2. **Overview of Botanical pesticides**

The term botanical derives from "botanic," which originates from the Greek word "*botanikos*" meaning "of herbs". Botanicals are conceptualized as plants or substances extracted from plants for various purposes, including skin and hair products, flavoring, and medicinal preparation. These plants provide a rich source of novel substances used to develop environmentally benign systems for controlling insect and pests (Jbilou *et al*., 2006). Consequently, such plants represent a fundamental basis for most natural products used today. For instance, about 62 % of the world's population largely depends on plant-derived medicines (Cragg *et al*., 2013), as plant derivatives contain extensively diversified bioactive compounds. These are described or identified as chemical molecules produced by living organisms and exert biological effects. Plant-based properties are termed secondary metabolites, which could be exploited by humans as raw materials for most products, like novel drugs (Pavela *et al*., 2016). Furthermore, the secondary metabolites produced by plants typically offer a form of resistance against diverse environmental pressures and found to show evidence of antiprotozoal, antiviral, antibacterial, and antifungal properties (Pérez *et al.,* 2016). For natural drug identification, the stages involve the screening of crude natural extracts with a suitable *in vitro* assay, followed by bioassay-guided fractionation of the potential extracts before isolation and purification of the bioactive constituent(s) (Cragg *et al*., 2005). After completing these processes, classification of the bioactive compounds is required.

Bioactive compounds are typically obtained by solvent extraction or other separation techniques. Solvent extraction is the most efficient because it easily solubilizes the needed compounds by penetrating and accessing the plant cells (Hernández-Ledesma *et al*., 2013). According to Shannon *et al*. (2016), polarity is crucial to this method, and determines how the extracts interact with the functional groups on the shell of the pathogen. Hydrophobic compounds are extracted by non-polar solvents, whereas the hydrophilic compounds are recovered with polar solvents. However, when the polarities of the bioactive compounds are unknown, a broad-spectrum solvent approach is the most suitable. Subsequently, the extracts are concentrated, formulated, and evaluated for effectiveness under controlled laboratory or field conditions (Zarubova *et al*., 2015).

Pesticides are substances, chemical compounds, or agents used to kill or destroy pests (Ivase *et al*., 2017; Williams, 1967). These chemicals are widely known for providing the most efficient, cost-effective and adept means of managing insect pests, fungi, weeds, and nematodes that vie for food crops in contemporary agriculture (Carvalho, 2017).The general term *pesticide* applies to a wide variety of chemicals including fungicides, herbicides, biocides, and rodenticides. Pesticides exist as either synthetic or bio-based substances. Synthetic pesticides are chemicals prepared in a laboratory to kill pests, and are broadly classified as organochlorines, organophosphates, carbamates, and pyrethrins (Carvalho, 2017; Williams, 1967). By contrast, biopesticides are natural pesticides obtained from living organisms, and categorized as microbial, plant-incorporated protectants, botanical pesticides, and pheromones (Figure 1). This paper focuses on botanical pesticides (BPs).

BPs are essential oils, extracted as secondary metabolites from parts or the entire plants. Typically, extracted metabolites have the potential to kill insects, pests, control weed, and sterilize instruments. BPs exist as either isolated substances or complex mixtures, which exert a range of biological effects by acting as repellents, insecticides, fungicides, bactericides, and nematicides (Isman, 2006). Numerous plants with pesticide properties have been investigated, identified, and isolated worldwide, as documented by scientific literature. Mwine *et al*. (2011) ascertained that 34 classes belonging to 18 families are utilized in customary agricultural techniques. Likewise, studies by Lajide *et al*. (1998) and Fatope *et al*. (1995) explored the defensive efficacy of selected local plants in Nigeria against weevil species *Sitophilus zeamais M*. and *Callosobruchus maculatus F*. in maize and cowpea. being used for traditional agricultural practices in developing countries.

Numerous studies and empirical results indicate that many screened plants possess pesticidal properties,

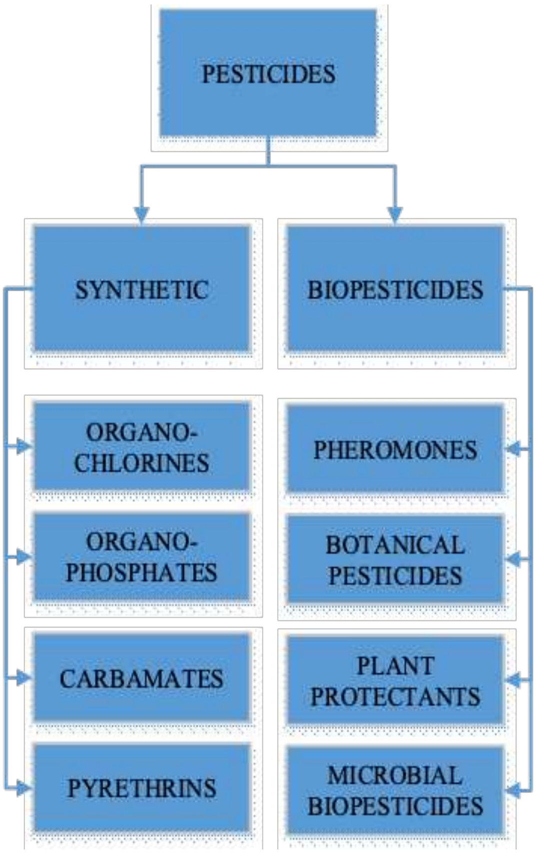

Figure 1. Grouping of Pesticides (Modified from Chengala *et al*., 2017).

Successful commercialization comes with acceptance, adoption, and utilization of these products in different countries. This requires, however, adequate proof and information regarding product chemistry and efficiency to meet national registration regulations (Isman *et al*., 2014). Such guidelines include information on design, breakdown, long life span, and harmfulness (Sarkar *et al*., 2014).

3. Standardization of Botanicals

Patel *et al*. (2006) considered botanical standardization as an important measure for ensuring the timespan and quality of botanicals. The authors further detailed that "standardization" helps to highlight the entire procedure, typically from production to quality control, which guarantees reproducible product quality. Ribnicky *et al*. (2008) observed that standardization is the manufacture of any plant preparation that has constant constituents and efficiency. Another conceptual view on standardization notes that it is the finest technological solution for consensual knowledge, which includes successive methods for selecting, safeguarding, and making secure decisions on approvals and achievable standards. Botanical standardization refers to the validation of its distinctiveness and the assessment of its quality and purity (Ninfali *et al*., 2009). It also involves detecting the nature of the adulterant *via* considering its morphologic, microscopic, biological, physical, and chemical properties (Phansalkar *et al*., 2017).

The study by Sharma *et al*. (2010) reported that the process of botanical standardization covers the whole field of study, starting from the plant origins to its applications. These measures are taken during the manufacture and quality control process to end up with reproducible quality products. Likewise, it is demonstrated as being the first step toward establishing a quality assurance program for manufacturing. Botanicals are extracted from the specific parts of plants responsible for the required pesticide activity (Isman, 2020). Unlike artificial pesticides that are acquired in their desired purity, BPs are not obtained with consistent purity from their raw materials, because of the wide fluctuations in active ingredient content in parts of plant, collected from various geographical zones. Hence, the raw materials require evaluation and standardization based on the contained compounds (Sarkar *et al*., 2014). Nonetheless, the process of standardization is challenging, since several features impact the bio-efficacy and reproducible pesticidal effect of BPs (Ninfali et al., 2009). The procedure for standardizing basic botanicals must consider (Sharma *et al*., 2010)

i. Authentication,
ii. Stability (Physicochemical parameters, such as quantitative and qualitative analysis, and microbiological assessment).

Authentication represents the initial step in botanical standardization. This phase involves the classification of plant species according to their Latin names or synonyms. Measures involved in this stage include taxonomic, microscopic, and macroscopic studies. Besides, one should use records from the collection stage of plant parts and the status of the collection region. Others include the botanical identity, like microscopic, Phyto-morphology, and histological analysis, such as stomata, trichomes, taxonomical identity, and quantitative microscopy. This list includes organoleptic evaluation, foreign matter, ash, extractives, and moisture contents. Lastly, spectrometer and chromatographic analyses, pesticide residue, heavy metal determination, radioactive and microbial contaminations require authentication (Sarkar *et al*., 2014; Sharma *et al*., 2010). Stability parameters (like microbiology, physical, and chemical) are basic features that yield reproducibility. Physical testing includes odor, color appearance, moisture content, viscosity, pH, and hardness, along with flocculation, settling rate, sedimentation, and ash values. Chemical parameters include chemical-based assays and limit tests. In addition, chromatographic analysis of botanicals is carried out using HPLC, TLC, GC, HPTLC, UV Fluorimetry, and GC-MS. Microbiological parameters take into account the total mold count, total viable content, and the total entero-bacterial counts. Further, limiters could be adopted as quantitative or semi-quantitative tools to institute and manage the total impurities. This is like the reagents used in generalizing diverse herbs and impurities from used solvents or the vessels used in manufacturing. Even so, to get hold of quality products, caution is required beginning with the suitable classification of plants, region, and time of gathering, as well as the selected processes for extraction and purification (Patel *et al*., 2006).

4. Quality Control of Botanicals

Botanical pesticides have been repeatedly disparaged for their uneven performance and lack of reliability. Hence, quality control (QC) is the key to guarantee safe delivery of effective end-products following the specification and prescribed conditions. Nevertheless, QC is defined as the processes involved in upholding the quality or validity of manufactured products (Mukherjee, 2002). With the suitable QC measures, there is an assurance that the botanicals enclosed in the box up are identical to what is stated on the label outside the package. Therefore, these procedures could serve as the starting point of constant manufacturing methods, once products are consistently made and QC measures included in the operations (Mena *et al*., 2018). QC functions cover all production phases. The study by Leppla (2003) showed that QC encompasses controls for production, processes, and product quality. Therefore, QC aims to establish the parameters for examining the progress of the process. Besides, it serves as prerequisite for the production and formulation of ingredients, receipt of raw materials, and outgoing end-use products. Although botanicals are frequently collected from their native environment, there is a point of worry over the consistency of the end-products. Hence, a reckless collection approach could lead to the ecological obliteration or endangerment of the plants, when it is not limited to research purposes (Techen *et al*., 2004). To establish the procedure, the specification of raw material, formulation of ingredients, and the end-product for usage, appropriate standards, and measurement methods must be ascertained. For instance, an organization can decide on its specific standards, although the final products should usually follow regulations. For botanicals, QC starts at the collection of raw materials from their source and ensuring the production equipment and its maintenance, which is termed the production control phase. According to Mena *et al*. (2018), this phase guarantees that the raw materials meet defined requirements, and that all manufacturing equipment is properly maintained.

Warrior *et al*. (2002) note that the quality of raw materials adds to the quality of the end-product. Hence, specification of raw materials needs to be cross-checked before commencing production. The author referred to the large-scale production of *Bacillus thuringiensis* (Bt) (Warrior *et al*., 2002). QC of the raw materials is essential because it ensures reproducible quality (De Smet, 2004). Various molecular methods like fragment restraint, length polymorphism, and DNA sequencing or chance intensification of polymorphic DNA may be adapted to validate the quality of raw materials and perceived adulterant plant species (Lum *et al*., 2005; Oszmianski *et al*., 1986). However, this technique varies in terms of accuracy, cost, time, reproducibility, and taxonomic level of identification. The second phase is known as the process control. This phase is intended to ensure that all production processes adhere to the recognized parameters, to ensure the anticipated yields and formulated products are supplied. Process control in production also relates to monitoring and guaranteeing that the vital process parameters are operated in agreement with credible profiles. Lastly, the product QC phase guarantees that the formulated end-use product adheres to the specifications, quality standards, and the required efficiency norms. Besides, this phase serves to depict conditions for its use and to meet the criteria set by the established national/international registration. QC is carried out on the materials and on packaging, which is a safe practice that does not to manipulate quality. The following parameters are timely tested to avoid losing storage time.

i. Number of infective propagates,
ii. Microbial contaminants,
iii. Physical-chemical properties.

Lastly, when the testing is concluded and results conformed, the products can be declared as safe for sample or use by consumers.

5. Bio-Enhancement of Botanicals

Bio-enhancement is a concept in modern science, initially described by Bose in year 1929. A bio-enhancer was disclosed, which served as a supplement, such as the anti-asthmatic effects of Vasaka (*Adhatoda vasica*) leaves, added to Long Pepper (*Piper longum*). It is also an agent with the capacity to improve the bioavailability and bio-efficacy of a drug or botany, when co-administered at low concentration. The concept is called Yogvahi in Ayurveda (Randhawa *et al*., 2011). The increased inaction of one biomolecule by another distinct chemical is the brand of poly-herbal formulations of Ayurveda. For BPs, the vigorous compounds inside the botanical formulations are frequently hydrophobic and may precipitate at high concentrations. Hence, the increase in BPs concentration to advance their bio-efficacy is counterproductive. Like synthetic drugs, the utilization of bio-enhancers and solubilizers is a logical approach for many botanicals (Ribnicky *et al*., 2008). This is because bio-enhancers increase the bioavailability of herbal pesticides during usage (Kesarwani *et al*., 2013).

6. Botanicals and Improvement of Human Health and Agriculture

Over-reliance on synthetic pesticides for pest control and diseases remains a leading technique in conventional agriculture. It is recognized that human health and the environment are prone to the dangers of current unsustainable agricultural techniques. Conversely, botanical pesticides (BPs) have been tipped as the best alternative pesticides to replace these chemicals. Many researchers have published comprehensive works on the irreversible damage of synthetic chemicals to human health, safety, and the environment (Dabrowski *et al*., 2014; Saruchi *et al*., 2016). Unfortunately, there are just a few studies on the impact of standardization, QC, and bio-enhancement of botanicals on agriculture and human health. The objective of standardization and QC is to offer clients a safe effective end-product, with high levels of the active constituent. Reproducibility of the standardized BPs guarantees safety by preventing the unintentional over application of pesticides and providing the consumer with predictable product efficacy. Hence, the incorporation of standardized BPs into farming encourages good agricultural practices (GAP). Furthermore, good quality raw materials ensure a major payback to the farmers, which includes improved quality of food products, food safety, market access, and cuts down pest levels thereby reducing the damage of stored corps (Nefzi, 2016). Integration of BIs into pest control and crop management programs could greatly lessen the negative outcomes of synthetic pesticides on the environment and human health.

7. Conclusions

There is an abundance of a broad variety of plants in our ecosystem. These plants form the crucial foundation for most natural products mankind uses today. Plant extracts for instance are used as start-up materials for herbal drugs and the production of pesticides. Due to dangers (environmental poisoning, harming of on targeted insects, and human health poisoning) posed by synthetic pesticides, it has become essential to search for eco-friendly and safe alternatives. BPs are unlikely to completely displace synthetic pesticides in the projected future given that there are too many hurdles hampering its commercialization and acceptance. However, where a price is placed on environmental safety and there is a higher broadmindedness for the presence of insects and/

or damage, then BPs could find growing acceptance of their usage. It is imperative to foster the transition from SPs to BPs, for the sake of environmental safeness and lives.

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