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Review

Botanical Biopesticides and Analysis of The Kenyan Legal Frameworks Regulating Biocontrol Agents: A Review

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Abstract: Before the green revolution, crude plant materials and plant-extracts were used for crop protection. However, their use was swiftly replaced by synthetic pesticides after World War II due to increased demand for more effective pesticides in intensified farming systems. The 20th century saw a steady increase in the use of synthetic pesticides until the mid-21st century when the world started to realize the negative impact of synthetic pesticides. The increased environmental awareness and the need for safe human food led to increased research and development of biopesticides as crop protection options in modern agriculture. This paper brings into perspective the global history of the application and use of botanical biopesticides in crop production. It also highlights the research progress, product development and registration challenges, and opportunities for business and adoption at the farm level in Kenya.

Keywords: biopesticides; formulations; fungicidal; pesticidal plants; plant extracts; regulations

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Introduction

Importance of plant diseases

The diversity of plant pathogens all over the globe includes fungi, bacteria, and nematodes that cause severe loss in terms of economics and production in the agriculture sector (Kannan *et al*., 2015). Fungal pathogens play a significant role in plant health (Yang *et al*., 2017). and as such, played a key role in driving technological advances in agricultural sciences from 1845 when the potato famine struck Ireland following successive crop failures (from 1845 to 1852) due to infection by *Phytophthora infestans* (Goyal & Manoharachary, 2014). Downy mildew (*Plasmopara viticola*) and powdery mildew (*Erysiphe necator*) nearly destroyed grapevine fields threatening wine production in many European countries. Potato late blight has remained the most important potato disease in Europe since its introduction from Central Mexico in the 19th century (Goss *et al*., 2014). Coffee leaf rust caused by the fungus, *Hemileia vastatrix,* Berk. and Broome, wiped out coffee in Ceylon (now Sri Lanka) (Hindorf & Omondi, 2011) and has continued to be the most significant disease of Arabica coffee in the world as well as one of the most studied plant pathogens (Talhinhas *et al*., 2017). Rust of wheat has caused a rise in yield losses, mitigation costs, and wheat import bans between countries (Suurbaar *et al*., 2017). The losses associated with wheat rusts called for wide-range studies in the genetics of plant disease resistance, the life cycle of plant pathogens, and host-parasite interactions (Muleta, 2007). To date, rust diseases have remained a major threat to wheat crops causing significant yield losses and reduced grain quality. The continued emergence of the Ug99 race of stem rust is of particular importance. There are three types of rusts disease affecting wheat: leaf rust (*Puccinia triticina* Eriks), stripe rust or yellow rust (*P. striiformis* Westend. f. sp. *tritici* Eriks), and stem rust (*P. graminis* Pers: Pers. f. sp. *tritici* Eriks) (Raja *et al*., 2017; Singh, 2014). Fungal plant diseases have continued to cause havoc among farming communities, with some causing significant economic losses or total loss of crops in some countries (Ahmad *et al*., 2010). Thus, world food production continues to be adversely affected by plant diseases during crop growth, harvest, and storage. Eliminating these diseases will go a long way in reducing the food crisis, thus enhancing food security.

Plant bacterial pathogens adversely caused significant agricultural impact as early as 1932 when bacterial spot was detected in peach orchards (Stefani, 2010). Since then, bacterial spot has been detected in stone fruit farms in various geographical areas. The most pathogenic bacteria species belong to genera such as *Erwinia, Pectobacterium, Pantoea, Agrobacterium, Pseudomonas, Ralstonia, Burkholderia, Acidovorax, Xanthomonas, Clavibacter, Streptomyces, Xylella, Spiroplasma*, and *Phytoplasma* (Kannan *et al*., 2015). For instance, *Erwinia* spp has been reported as one of the most important bacterial diseases causing several diseases in several economically important plants and is referred to as the premier phytopathogenic bacterium (Kannan *et al*., 2015). These bacteria are widespread in many production areas worldwide and degrade pectin causing soft rot diseases. The phytopathogenic *Agrobacterium* has a worldwide impact and has been reported to cause significant losses in fruit trees, nuts, grapevines, vegetables, and ornamentals such as roses and chrysanthemums (Pulawska, 2010). The losses associated with this disease in nurseries may go up to 30%, and the crops may not be fit for market. *Ralstonia solanacearum* infects over 200 plant species in more than 50 families and causes diseases such as potato brown rot, tobacco, eggplant, several ornamental bacterial wilts, and banana moko disease. *R. solanacearum's* direct economic impact is difficult to quantify, but given its extensive geographic spread and host range, this disease is quite destructive. *Xanthomonas* spp causes at least 350 diseases with rotting symptoms, resulting in tremendous economic losses in agriculture. *Xanthomonas* species have numerous pathovars that affect various economically significant host plants and cause important diseases (Mansfield *et al*., 2012).

Plant parasitic nematodes cause damages of 157 billion dollars worldwide (Singh *et al*., 2015). They damage the host plant by causing wounds on the plant roots forming brown spots on the root, and swelling or rotting of the tubers (Bernard *et al*., 2017). The most successful plant-parasitic nematodes are the sedentary groups, which establish a stable feeding site within the plant host and absorb nutrients while completing their lifecycles. Sedentary nematodes have a natural advantage over their migratory relatives due to a fascinating and sophisticated host cell transformation that results in a sustained feeding structure. The topmost important plant parasitic nematodes include root-knot nematodes (*Meloidogyne* spp) comprising *Meloidogyne javanica, Meloidogyne arenaria, Meloidogyne hapla,* and *Meloidogyne incognita* representing the most devastating threat to agricultural crop production. Cyst nematodes (*Heterodera* and *Globodera* spp) come second, as they damage vascular tissues, weakening them and causing stunting and discolour. Potato cyst nematodes are an example and have been reported to cause crop failure and financial losses to farmers (Mburu *et al*., 2020). Lesion nematodes (*Pratylechus* spp), with a worldwide distribution with a host range of nearly 400 plants, are considered major economic significance in cereals. (Smiley, 2015). Four *Pratylechus* spp, *P. thornei, P. neglectus, P. penetrans,* and *P. crenatus*, are the most important and widely distributed. *Pratylechus thornei*, on the other hand, is thought to be more damaging, causing yield losses of up to 50% in the United States and 85% in Australia. (Mokrini *et al*., 2018). The lesion nematodes are migratory, feed on the root cortex, and may enter vascular tissues to obtain nutrients. Burrowing nematodes (*Radophlus similis*) are listed as a quarantine pest hosted by over 250 plant species. *R. similis* damages banana, citrus, pepper, coffee and other crops and is considered the most important phytopathogenic nematode in banana-growing areas.

Bio-Pesticides

Biopesticides are compounds or organisms that occur naturally with low risks and are used to control pests and diseases (Kansiime *et al*., 2017). According to Suman and Dikshit (2010), biopesticides are a diverse group of microbial pesticides and biochemicals derived from microorganisms and natural sources. They are effective, biodegradable with no residuals to the environment (; Chandler et al., 2011, S. Sharma & Malik, 2012: Kachhawa, 2017; Kutawa et al., 2016; Arjjumend & Koutouki, 2018). They are either made from parts (phytochemicals, microbial products), by-products (Semiochemicals) or whole living organisms (natural enemies) (Kachhawa, 2017; Kutawa et al., 2016; S. Sharma & Malik, 2012). Plant-based biopesticides were used for crop protection by the Greeks, Romans, and Egyptians (Alburo & Olofson, 1987; Raghavendra et al., 2016) long before the agrarian revolution (Figure 1).

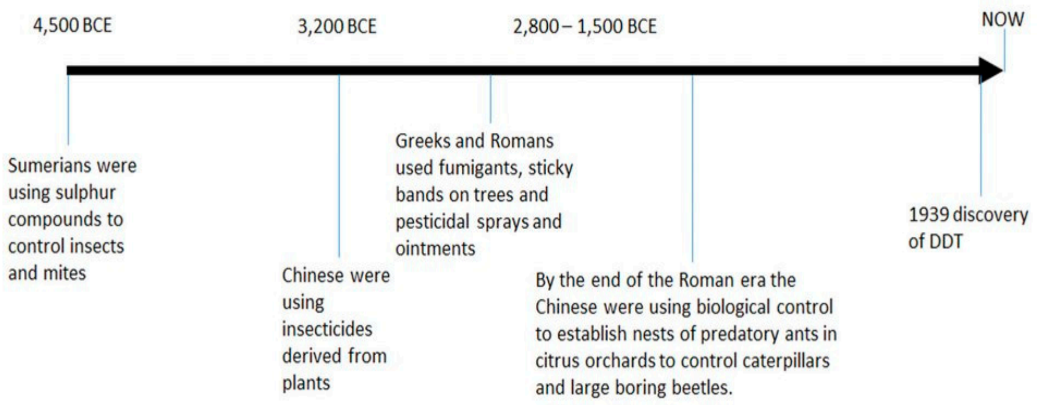

Figure 1. Timeline of the development of pesticides (Handley, 2019).

a) Microbial biopesticides

These are derived from microorganisms and their metabolites (Chandler *et al.*, 2011). Studies have reported over 3000 bacteria, 1000 viruses, 800 fungi, 1000 protozoa and 67 nematode species, all entomopathogenic to crop pests (Arjjumend & Koutouki, 2018; Holmes *et al.*, 2019; Kutawa *et al.*, 2016; Ruiu, 2018). These microbial biopesticides offer an alternative to synthetic insecticides with high specificity plus ecological safety (Kansiime *et al.*, 2017). The most successful and widely adopted of these is the bacterium *Bacillus thuringiensis* Berliner (Bt), which produces a crystal protein during bacterial spore formation capable of causing lysis of gut cells when consumed by susceptible insects (Speckbacher & Zeilinger, 2018). Currently, around 400 Bt formulations have been registered as biological control products and may be applied directly in sprays. Other microbial biopesticides include *Trichoderma harzianum*, *Coniothyrium minitans*, the K84 strain of *Agrobacterium radiobacter* used to control crown gall, *Bacillus subtilis*, *Pseudomonas fluorescens* and *Pseudomonas aureofaciens*. Microbial biopesticides are specific, nonpathogenic to wildlife, humans and other organisms, can be established in a pest population and can also be used as root and plant growth regulators. However, these biopesticides have their limitations as well. When exposed to heat, they lose efficacy and are only toxic to specific pests. Because they require unique formulations and storage procedures, there may be complications in the production and distribution of these pest control products (Kansiime *et al.*, 2017).

b) Macrobial biopesticides

Under the changing agricultural environment, biological control agents (BCA) remain one of the preferred technologies promising to manage plant diseases without disturbing the environment's and ecosystem's composition. Macrobial biopesticides achieve crop protection through the effect of macro-organisms classified as natural enemies, such as parasites, predators and parasitoids (Kutawa *et al.*, 2016; Sharma & Malik, 2012). Dozens of predators and parasitoids are reared worldwide and have been economically significant in managing plant pests and diseases. The production of parasites or predators, fungi, protozoa, bacteria, viruses, sterile males, or genetically incompatible individuals has become integral to biological control programmes. Laboratory stocks or those for mass production are derived from a small amount of field materials which are further inbred for many generations and can be released in the field. During this process, the genetic variability of the stock reduces while the adaptability to different environmental conditions improves. Therefore, effort should be made to maintain or increase genetic variability in mass-propagation programmes in an efficient way.

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c) Semiochemicals

These natural chemical signals produced by an organism affect another organism of the same or different species (Chandler *et al*., 2011; Koul, 2011). They can be volatile or non-volatile signals that operate long or short-range to modify the recipient's behaviour (Singh, 2014). They usually induce behavioural changes as attractants, repellants or mating disruptors (Holmes et al., 2019). Semiochemicals provide alternative solutions to synthetic pest control products. However, the product development process takes a long time and constitutes only a small fraction of the market (Arjjumend & Koutouki, 2018). Some semiochemical-based control methods commercially available include attractants or stimulants, arrestants, repellents and deterrents. The most widely used semiochemicals for crop protection are sex pheromones, which can be synthesized and used for monitoring or pest control by mass trapping, lure-and-kill systems, and mating disruption (Chandler *et al*., 2011).

d) Plant Incorporated Protectants (PIP)

These are biopesticide substances produced by plants from genetic material that have been added or incorporated into their genetic make-up, e.g., Bt protein (Chandler *et al*., 2011; Damalas & Koutroubas, 2018; Gupta & Dikshit, 2010; Kutawa *et al*., 2016; K. R. Sharma *et al*., 2018). When plants are genetically modified to produce a pesticide, they are regulated as pesticides by Environmental Protection Agency (EPA) in the USA and National Biosafety Authority (NBA) in Kenya and as plant products under EU plant protection regulations. Hence, the pesticide produced by such plants and the genetic material introduced are defined as PIPs. To date, scientists have had a lot of focus on the use of virus coat protein and replication genes for genetic engineering by incorporating them into plants. Several breeding programs across the globe have successfully incorporated genetic material into various crops for disease resistance as a long-lasting disease management strategy.

e) Botanical biopesticides (Plant Extracts)

Botanicals or plant extracts are plant derivatives that can be used to control crop pests and diseases. Plant extracts were used to control crop insect pests long before the green revolution by the Greeks, Egyptians and Romans (Alburo & Olofson, 1987; Pavela, 2016; Raghavendra *et al*., 2016). However, after DDT's discovery, botanical biopesticides' use decreased significantly in the 20^{th} century (Pavela, 2016). The 20^{th} century was characterized by the significant development of synthetic pesticides, mainly pushed by the need for more food due to the increasing human population and more pesticides due to intensified farming systems and economic pressure (Oberemok *et al*., 2015). Synthetic pesticides are easier to use and highly effective, which fuels further industry growth (Oberemok *et al*., 2015). The intensive crop production systems led to the excessive use of synthetic pesticides negatively impacted humans and the In the last three decades, global concern on the safe use of pesticides, food safety, and environmental degradation has led to a significant shift from synthetics to biopesticides (Damalas & Koutroubas, 2018). This change in preference and consumer demands has also resulted in increased adoption of plant extracts in Integrated Pest Management (IPM) options and organic farming systems.

Botanical pesticide plants are readily and commercially available, with most having multiple uses, such as medicines, spices, ornamentals, and organic soil amendments. Studies have reported antimicrobial effects of products from neem, custard apple, garlic, and ginger, among other medicinal plants. These can be applied as secondary metabolites, crude extracts or powder of dried plant parts (Choudhury et al., 2018). Commercialized pyrethrum, neem, and sabadilla biopesticides are less toxic to beneficial and non-target organisms, making them acceptable and reliable in a sustainable production system.

Mechanisms of pest control of biopesticides

The antimicrobial activity of botanical biopesticides is based on plant bioactive compounds, mainly secondary metabolites, which are usually affected by genetic structure and environment (Murtaza *et al*., 2015). Extracts for control of phytopathogens have mainly been obtained from plant species such as *Aloe vera*, Eucalyptus (*Eucalyptus globulus*), neem (*Azadirachta indica*), and herbaceous

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species like garlic (*Allium sativum*), mint (*Mentha spicata*), ginger (*Zingiber officinale*). These plants synthesize aromatic secondary metabolites like phenols, phenolic acids, quinones, flavones, flavonoids, flavanols, tannins and coumarins. The compounds containing phenolic structures, such as carvacrol, eugenols, and thymol, are highly active against plant pathogens and serve as plant defence mechanisms against plant pathogenic microorganisms (Table 1). However, their efficacies differ based on diversity in the chemical bio-composition, such as the secondary metabolites of plants. The antimicrobial activity of medicinal plants may be because of the synergistic activity of diverse bioactive metabolites that may act as antiseptic, cicatrizant and antiparasitic (Fyhrquist, 2007). These compounds are classified into four classes: - Terpenoids, Saponins, phenolic compounds and flavones, flavonoids and flavonols.

Global Research Progress on the Use of Plant Biopesticides to Control Crop Diseases

Various studies have been carried out on the efficacy of botanical biopesticides against plant pathogens. Though the success has been low compared to synthetic pesticides, there are some novel documented success stories across the globe (Table 2).

Table 1. Common classification of phytochemicals and the modes of action.

Class	Sub-Class	Description	Mechanism of control	References
Phenolic compounds	Simple and alkylated phenols	Plant defence mechanisms against pathogens and insects.	-Membrane disruption, substrate deprivation	(Bhardwaj *et al*., 2015; Choudhury *et al*., 2018)
	Phenolic acids	Aromatic acids that contain a phenolic ring and a carboxyl functional group	-Bind to adhesins, forms complex with the cell wall, inactivate enzymes	(Altemimi *et al*., 2017; Draz *et al*., 2019; Dulf *et al*., 2017; Kurmukov, 2013; Pharmacopeia, 1998)
	phenylpropanoids coumarins, quinines, anthraquinones, xanthones	Aromatic plants mainly produce them and have antifungal and antibacterial properties	- Interaction with eucaryotic DNA	(Al-Huqail *et al*., 2019; Gurjar *et al*., 2012; Monteiro *et al*., 2016).
	Tannins	Astringent, polyphenolic biomolecules	Bind to and precipitate proteins, enzyme inhibition, substrate deprivation	(Gurjar *et al*., 2012; Koche *et al*., 2016; Kurmukov, 2013; Salhi *et al*., 2017)
Terpenoids (Isoprenoids) sesquiterpenes, diterpenes, diterpenoids, triterpenoids	Essential oils prenyllipids	These are the oldest group of small molecular products synthesized by plants and the most widely spread.	Cell membrane disruption	(Bhardwaj *et al*., 2015; Koche *et al*., 2016; Kurmukov, 2013)
Alkaloids		Basic, naturally occurring organic compounds that contain at least one nitrogen, such as morphine or caffeine	Intercalate into cell wall	(Koche *et al*., 2016; Salhi *et al*., 2017)

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Flavones, flavonoids and flavonols-		Plants synthesize them in response to microbial infections. They are phenolic compounds with one carboxyl group.	Bind to adhesins, forms complex with the cell wall, Inactivate enzymes	(Kurmukov, 2013; Salhi *et al*., 2017; Uwague, 2017)
Lectins and Polypeptides		Carbohydrate-binding proteins that are highly specific for sugar groups that are part of other molecules	Form disulfide bridges Cause agglutination	(Freire *et al*., 2012)
Saponins		Constitutive antifungal plant metabolites that act as natural detergents chemically related to triterpenes saponins and steroidal saponins	- antimicrobial, cholesterol-lowering, and anti-cancer. The main compound produced by cayenne pepper.	(Kurmukov, 2013; Salhi *et al*., 2017)

Table 2. Examples of plants with antimicrobial effects and the pathogens they control.

Plant	**Common name**	**Target pathogen**	**Reference**
Datura stramonium	Datura	*Puccinia triticina* Eriks *Alternaria solani* and *Fusarium oxysporum*	(Chaudhary *et al*., 2015; Draz *et al*., 2019; M. Rahman *et al*., 2009), (Jalander & Gachande, 2012)
Acalypha wilkesiana	Acalypha	*Puccinia triticina* Eriks	(Draz *et al*., 2019)
Lawsonia inermis	Henna	*Puccinia triticina* Eriks	(Ambikapathy *et al*., 2011; Draz *et al*., 2019)
Melia azedarach	Chinaberry	*Puccinia triticina* Eriks	(Draz *et al*., 2019)

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Punica granatum	Pomegranate	*Puccinia triticina* Eriks	(Draz *et al.*, 2019)
Lantana camara	Lantana	*Puccinia triticina* Eriks	(Draz *et al.*, 2019)
Allium cepa	Onion	*Helminthosporium turcicum* and *Ascochyta rabiei*	(Gwa *et al.*, 2018)
Calotropis procera	Giant milkweed	*Helminthosporium turcicum* and *Ascochyta rabiei*	(Gwa *et al.*, 2018)
Adenocallima alliaceum	garlic vine	*Alternaria alternate* and *Fusarium oxysporum*	
Zingiber officinale	Ginger	*Penicillium expansum*	(Gwa *et al.*, 2018; Parveen *et al.*, 2014)
Piper nigrum	Black pepper	*Penicillium expansum*	(Gwa *et al.*, 2018)
Azadirachta indica	Neem	*Penicillium expansum*, *Pectobacterium carotovorum subspecies carotovorum*, *Pectobacterium atrosepticum*, *Dickeya dadantii*, *Oidium anacardia*, *Phytophthora infestans* and *Rhizoctonia infestans*	(Gwa *et al.*, 2018; Ngadze, 2013; Paradza *et al.*, 2013; Shomari & Menge, 2013)
Nicotiana tabacum	Tobacco	*Penicillium expansum*	(Gwa *et al.*, 2018; Jangam *et al.*, 2014; S. Rahman *et al.*, 2016)
Acacia saligna (Labill.) H. L. Wendl.	Golden wattle	*Rhizoctonia solani, Fusarium culmorum* and *Penicillium chrysogenum*	(Al-Huqail *et al.*, 2019)
Xylaria spp		*Botrytis cinerea*	(Adongo *et al.*, 2013)
Allium sativum	Garlic	*Pectobacterium carotovorum subspecies carotovorum, Pectobacterium atrosepticum Dickeya dadantii, Phytophthora infestans* and *Rhizoctonia infestans*	(Ngadze, 2013; Paradza *et al.*, 2013)

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Morinda morindoides, *Senna occidentalis* *Opuntia cactus* *Opuntia vulgaris*	- - - -	*Oidium anacardii*	(Shomari & Menge, 2013)
Carica papaya	Pawpaw	*Colletotrichum kahawae* L., *Phytophthora infestans* and *Rhizoctonia infestans*	(Ngadze, 2013; Ngouegni *et al*., 2017)
Tagetes minuta *Vinca rosea*	Mexican marigold Periwinkle	*Phytophthora infestans* and *Rhizoctonia infestans*	(Ngadze, 2013)
Artemisia herba alba *Cotula cinereal* *Asphodelus tenuifolius* *Euphorbia guyoniana*	desert or white wormwood Onion weed Euphorbia	*Fusarium graminearum* and *Fusarium sporotrichioides*	(Salhi *et al*., 2017)
Phyllanthus amarus Schum. and Thonn.	-	*Aspergillus niger, Aspergillus flavus, Fusarium oxysporum,* and *Rhizopus stolonifera*	(Sen & Batra, 2012)
Lawsonia inermis L. *Mimosa pudica L.* *Phyllanthus niruri L. Tephrosia purpurea Pens.* *Vinca rosea L.*	-	*Pythium debaryanum*	(Ambikapathy *et al*., 2011)
Cymbopogon citratus	-	*Colletotrichum kahawae* L., *Ustilago maydis, Ustilaginoidea virens, Curvularia lunata, and Rhizopus spp*	(Ngouegni *et al*., 2017)
Eucalyptus saligna	-	*Colletotrichum kahawae* L.	(Ngouegni *et al*., 2017)
Phenopodium ambroides	-	*Rhizoctonia solani*	(Singh, 2014)
Chromoleana odorata *Xylopia aethiopica*	-	*Ustilago maydis, Ustilaginoidea virens, Curvularia lunata, and Rhizopus spp*	(Singh, 2014)

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Leonotis nepetifolia L.	-	*Phoma exigua*	
Ocimum gratissimum L.	-	*Phoma exigua, Ustilago maydis, Ustilaginoidea virens, Curvularia lunata, and Rhizopus spp*	(Singh, 2014)
Pelargonium odoratissimum	Apple geranium	*Erwinia armylovora*	(Chiriac and Ulea 2012)
Salvia officinalis	Sage	*Erwinia armylovora*	(Chiriac and Ulea 2012)
Tagetes minuta	French marigold	*Erwinia armylovora*	(Chiriac and Ulea 2012)
Hedera helix L	Ivy	*Erwinia armylovora*	(Baysal and Zeller, 2004)
Syzygium aromatcum	Clove	*Erwinia amylovora* *Xanthomonas arboricola pv. corylina, Xanthomonas arboricola pv. juglandis, Pseudomonas syringae pv. Syringae* *Agrobacterium tumefaciens*	(Mikicinski *et al.*, 2012)
Origanum compactum	Oregano	*Erwinia amylovora* *Pseudomonas syringae pv. Syringae, Pseudomonas fluorescens,* *Pantoea dispersa* *Pantoea agglomerans*	(Kokoskova *et al.*, 2011)
Thymus vulgaris	Thyme	*Erwinia amylovora* *Pseudomonas syringae pv. Syringae, Pseudomonas fluorescens,* *Pantoea dispersa,* *Pantoea agglomerans*	(Kokoskova *et al.*, 2011)
Origanum vulgare	Wild oregano	*Pseudomonas syringae pv. garcea*	(Kokoskova *et al.*, 2011)
Ocimum tenuiflorum	Holy basil	*Xanthomonas axonopodis pv. punicae*	(Sherkhane *et al.*, 2018)

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Regulation and Policy Framework of Biopesticides

Globally, various regulatory bodies and agencies such as International Organization for Biological Control (IOBC), the European and Mediterranean Plant Protection Organization (EPPO) and Organization for Economic and Co-operative Development (OECD) have been involved in resolving registration impediments faced by countries (FAO, 2012). Over the past ten years, there has been an increase in the usage of bio-based products among farmers to manage pests and diseases in crops (Arora *et al*., 2016). However, the commercialization of these plant protection products is a rigorous process that necessitates testing and registration, which can be difficult with underdeveloped regulatory frameworks (AATF, 2013). Even in countries with well-developed regulatory frameworks, issues persist since existing regulations mainly apply to conventional chemicals rather than biological pesticides. Establishing competent biopesticide guidelines is critical for safety and ensuring minimal restrictions on biopesticide commercialization (Guest, 2015). According to AATF (2013), it is crucial to develop robust systems for the registration of biopesticides based on scientific data, standards and working registration systems. Registering these biopesticides is critical to such regulatory regimes, ensuring that only approved pesticides are registered. Biopesticides are utilized worldwide, although the regulatory processes and agencies involved differ at the regional and national levels.

Various African countries have developed or are developing regulatory systems for biopesticides as part of an Integrated Pest Management (IPM) strategy. In each of these countries, various organizations have the authority to regulate emerging biopesticides. For instance, in South Africa, laws and guidelines for regulations of registration and commercialization of biological control agents are under the Department of Agriculture, Forestry and Fisheries (DAFF) under the Act 36 of 1947 (DAFF 2010), while in Nigeria, National Agency for Food & Drug Administration (NAFDAC) is the agency mandated to regulate manufacturing, selling and distribution of fertilizers, biofertilizer and biopesticides. Closer home, in East Africa, in Tanzania, the regulatory body is the Tanzania Plant Health and Pesticides Authority (TPHPA) under the Ministry of Agriculture established by Act No. 4 of 2020 to comply with the requirements of the International Plant Protection Convention (IPPC) (Stadlinger *et al*., 2013). In Uganda, the National Agricultural Chemicals Board (UNACB) and the Agricultural Chemical Control Committee (ACCTC) are mandated by Ugandan laws to inspect and certify agrochemical trade (Arora *et al*., 2016).

The regulation of pesticide use and distribution is made through registration, legislation and enforcement of laws governing pesticides. Among East African countries, Kenya has well-developed biopesticides-specific registration legislation and mechanisms that ensure accurate assessment of the safety and dangers associated with microbial pesticides (Arora et al., 2016; Kabaluk et al., 2010). The Pest Control and Products Board (PCPB) is the regulatory body mandated to register all pest control products. It is supported by stakeholders such as the UK DFID (Kabaluk *et al*., 2010). PCPB was created through an act of Parliament, the Pest Control Products Act, Cap 346, Laws of Kenya which was enacted in 1982 (PCPB, 1985). This organization, therefore, regulates the importation, exportation, manufacture, distribution and use of products to control pests. The Pest Control Products Act also provides for registration and regulations for microbial pesticides (Wabule *et al*., 2004); (Kimani, 2014). The Kenya Plant Health Inspectorate Service (KEPHIS), through the Act, Cap 512 of 2013, and Plant Protection Act, regulates the imports and exports of live organisms. The act provides for application for introducing microbial and macrobials through KEPHIS, where the Kenya Standing Technical Committee on Imports and Exports (KSTCIE) operates under Cap 324 and advises the importer of the requirements and the areas to be addressed by the applicant.

Biopesticides development process

The process of biopesticide development involves two phases (Figure 2). Phase I involves the research and product development guided by regulations within the country of origin. This process is usually done under strict and controlled environments in research facilities. The experimental step begins with collecting and isolating potential microbes or fortifying the microorganisms, followed by

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identification, characterization and performance of efficacy bioassays (Mandakini and Manamgoda, 2021). Once a potential microorganism is identified for biopesticide production, it is accurately identified and characterized. Efficacy bioassays can be *in vitro*, *ex vivo*, or *in vivo*, depending on the target pathogen or pest organism, and pilot trials under actual application conditions. Phase II entails mass production, formulation, field testing and safety evaluation. Here several steps are involved with product and process development. Formulations are developed in the laboratory and pilot facilities which are scaled in manufacturing facilities (Strobel and Daisy, 2003). Field studies are conducted and data are gathered for the regulatory submissions supporting product registration (USDA, 2017a). Finally, biopesticides can be registered and introduced to the market upon completing safety evaluation and regulatory approval.

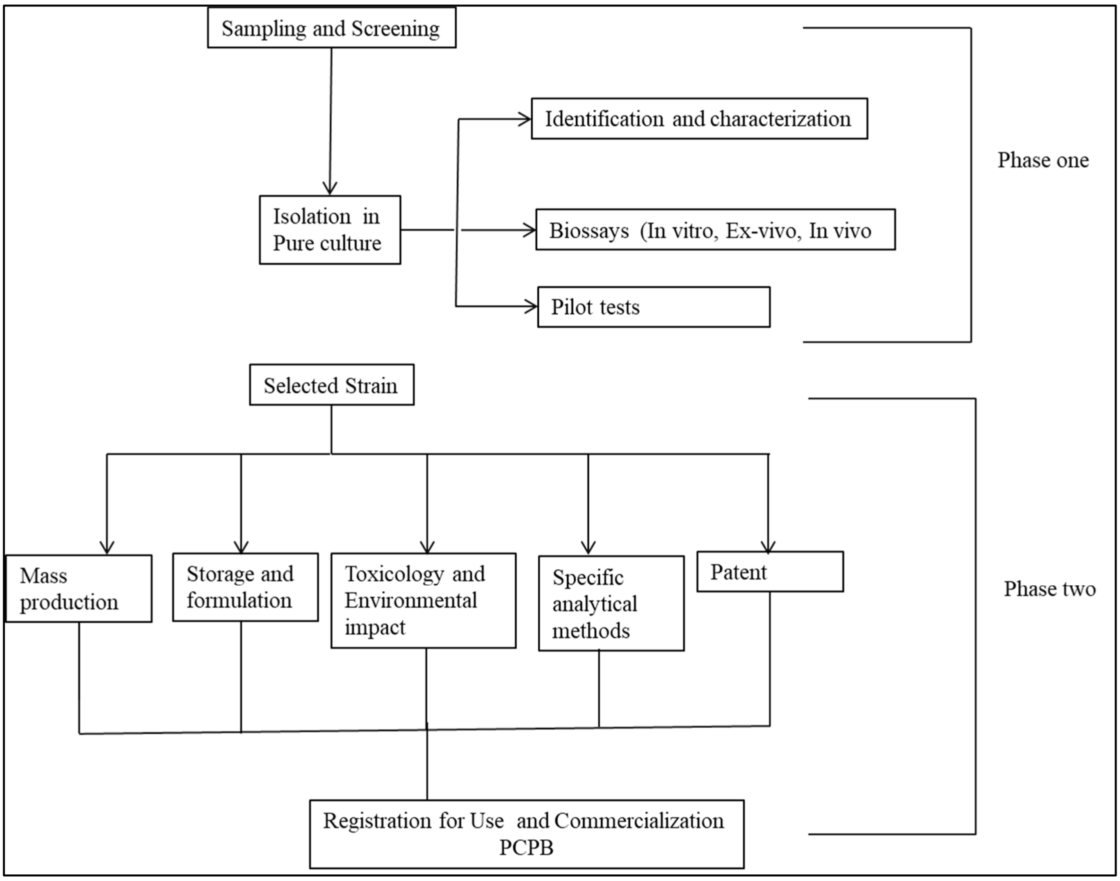

Figure 2. Regulatory and development processes.

Analysis of the Kenyan Legal Framework on Biocontrol Agents

All pesticides, including biopesticides for use in Kenya, are regulated by the Pest Control Products Board (PCPB), a statutory organization established in 1985 under Cap 346 Laws of Kenya. The Board is mandated to oversee all matters related to pesticides, including but not limited to regulation on importation and exportation, manufacture, distribution, sale and use of pest control products while mitigating their harmful effects on human health, animal health and the environment.

a) Registration process

The registration process of pesticides in Kenya is governed by the Pest Control Products Act (PCPB) Cap 346 of the Laws of Kenya. The act defines a pest control product as a product, device, organism, substance or thing manufactured, sold or used to directly or indirectly control, destroy, attract or repelling any pest. Biopesticides can be categorized into five major classes: microbial pesticides, biochemical pesticides, botanical pesticides, natural enemies and plant-incorporated protectants. The board considers pest control products' safety, efficacy, quality, and economic value in line with the registration regulations LN46/1984. To facilitate the registration and adoption of biopesticides, a face-to-face pre-submission consultation between the applicant/registrant and the registration authority (PCPB) is recommended. The registrant provides summary data containing details of the biopesticide, origin of the active agent, deposition of culture in a nationally recognized culture collection, any non-microbial active ingredients, and proof of ownership of the microbial biopesticides to be registered. A decision must be made on whether to grant registration according to the completeness of the data and a satisfactory outcome of risk assessments. In the case of an application for a complete registration, the registration authority may decide to grant provisional approval if further data are required. This situation may arise with a new product with insufficient field use experience. For regulation purposes, local efficacy trials should be conducted following the laid down procedures and data generated.

b) Current status of registration of biopesticides

The Pest Control Products Board (PCPB) has registered various pest control products. Over the last decade, there has been an increase in the number of applications for registration of biopesticides because of the maximum residue limits concerns locally and in the European and other export markets (Ngaruiya, 2004). As at now, ninety-one (91) biopesticides are listed at the PCPB website as fully registered (www.pcpb.go.ke/biopesticides-on-crops/)

Formulation of Botanical biopesticides

Over 20% of known plants have been used in pharmaceutical and crop protection studies across the globe. This has been facilitated by the high number of diverse bioactive compounds found in plants (Altemimi *et al*., 2017). For these products to be successfully utilized, they have to be extracted and formulated into forms that can be easily applied on plants as well as increase their shelf life (Marrone, 2007). However, according to Gasic and Tanovic, (2013) acceptable formulations are difficult to develop and this is mainly because the formulated product must keep its original biological function throughout storage and application. The formulation process leads to a final product by mixing with different carriers and adjuvants for survival as well improved bioactivity and storage stability (Hynes *et al*., 2011). Many of these biopesticides are based on living organisms and their viability must be maintained at levels that are acceptable during formulation and storage (Gasic and Tanovic, 2013). The development of biopesticide formulations that are both effective and safe is an important step in integrating this technology into integrated pest management systems (Hynes *et al*., 2011). However, the formulation type is determined by the biocontrol agent's mode of action and the stage at which the host plant is most vulnerable to the agent. Formulation can be done through extraction methods by use of solvents such as methanol, hexane, ethyl alcohol; microwave-assisted extraction which involves the use of electromagnetic radiation in the range of 300mHz to 300GHz; and the most efficient and effective being Ultrasonic assisted extraction which uses ultrasound (>20kHz) to lyse cell walls. Isolation and purification techniques of active ingredients can be done through paper chromatography, column chromatography, High-performance liquid chromatography (HPLC) and InfraRed while identification is done using Nuclear magnetic resonance and mass spectrometry. Hynes et al. (2011) when formulating granula biopesticide of bacteria and fungi employed extrusion –spheronization fluidized bed drying. Most biopesticides are formulated as dry (solid) formulations for direct application and they include dusts (DP), wettable powders (WP), and Granules (G). Liquid biopesticides formulations for dilution in water with adjuvants, protectants and nutrient and they include emulsions, suspension concentrates (SC) (Bharti and Ibrahim, 2020). Others are called inerts whose components are other than the active ingredients or microorganisms (Teicher, undated)

Safety, toxicity, and application of Botanical biopesticides

The toxicity level of pesticidal plants is not as high as that of most synthetic pesticides. However, pesticidal plants still contain toxic compounds. Thus, care and safety measures should be applied by both users and consumers. For several plants, the active ingredients are well known, with solid evidence of relatively low toxicity, such as rotenoids, azadirachtin and pyrethrin (Branco, 2011; FRAC, 2018; Pavela, 2016; Singh, 2014; Tembo *et al*., 2018). Risks of toxicity are further mitigated in that the amount of active ingredients naturally found in parts of plants is often low and certainly not present in the artificially concentrated amounts found in synthetic pesticides. Many of the compounds in pesticidal plants are also found in food and medicines, notably herbs and spices, from which essential oil pesticides are made. The USA has categorized them as GRAS (generally regarded as safe) and not subject to toxicity testing requirements. It is nevertheless essential to remember that plants contain toxins and to use appropriate safety measures such as gloves, face masks, and protective clothing. Exercise caution when processing, grinding, sieving plant powders, and applying them to crops. The Biocontrol products can be used as bait sprays for pheromone baits, spraying in the case of Bt-related products, the release of parasitoids and predators on crops, application as droplets in the case of baculoviruses, other biopesticides such as mycoinsecticide can be applied in an oil formulation (Gan-Mor and Mathews, 2003). Users of the products should avoid inhaling powders or contact with skin and eyes. In case of accidental contact, the affected area should be washed with clean running water.

Challenges and Drawbacks to Uptake of Botanical Biopesticides

Development, utilization, and promotion of Plant-based protectants, like other crop protection products, face challenges at various levels. Development is hampered by high costs of product development, legal restrictions, limited availability of germplasm, product formulation and short shelf life of the products (Chandler *et al*., 2011; Holmes *et al*., 2019). Utilization is minimal among farmers because the products are usually specific to pests, while the users prefer broad-spectrum products to minimize the costs of applications. This is further curtailed by the ability of the products to control pests at only specific growth stages and specific dosages. This, therefore, renders them less preferred as farmers have to buy and apply several products as opposed to synthetic pesticides (Arjjumend & Koutouki, 2018; Kutawa *et al*., 2016; Marrone, 2007). there is a need for coordination in developing biopesticides to address the challenges through research, which requires skilled human resources and adequate physical infrastructure. There is also a need for greater interaction and collaboration between various disciplines and sectors. The adoption can be enhanced through advocacy and integration with other pest management practices.

Opportunities for the Growth of the Botanical Biopesticides Industry

Based on earlier studies by Glare *et al*. 2016; Glare *et al*. 2012; Koul (2011), biopesticides were set to increase worldwide. An assessment by Travis *et al*. (2016) put the increase to 15% annually worldwide; as such, biopesticides may be entering a new era of mainstream use. In the last decade, there has been an increase in the range of registered biopesticides. Larger companies are acquiring small-sized ones, which indicates the growing market (Glare et al., 2016). Many countries have or are developing regulatory processes; however, the regulatory processes for one country may not fit the specific needs for microbial-based requirements for another country. Harmonization of regulations and development of particular guidelines for biopesticides assessment hamper the development and commercialization of biopesticides. As demonstrated by the increasing sales, the future of biopesticides is promising; however, there is a need to develop a policy framework that will support commercialization and remove barriers to commercialization on a global scale.

Policy Framework and business environment

Policy changes in Europe and elsewhere requiring more detailed safety data and maximum residue limits for synthetic pesticides may have changed the commercial interest in plant-based pesticides. Some countries such as China, India and Brazil have created favourable regulatory frameworks and have subsequently observed considerable growth in registered and commercialized plant-based pesticides (Arjjumend & Koutouki, 2018). Similar efforts need to be pursued by other countries worldwide. In Africa, strong heritage and ongoing use of plants as pesticides exist, particularly in smallholder agriculture (Singh, 2014). In addition, until relatively recently, East Africa was the leading global provider of crude pyrethrum. Therefore, there is great potential for natural pesticide development in Africa, towards which many African governments, policymakers and scientists can create the enabling regulatory and promotional environments required to encourage and facilitate entrepreneurs wanting to develop local practices into sustainable value chains for commercialized natural pest control products.

Research and development

Though research on plant-based pesticides has been ongoing for decades in Kenya, there has been limited focus and support for research in this area. Most of the research work has not been moved from the laboratory to the field due to a lack of suitable infrastructure, equipment and motivation to facilitate this level of research. Most of the research has been on using crude extracts of the plants and whole plant parts. However, this is not practical when it comes to adoption and application by farmers due to low efficacy and shelf life. There is a need to invest in the research and development of commercial products by refining research outputs into suitable formulations and toxicity studies. Governments must also deliberate efforts to facilitate the process of Intellectual property protection, research enablers/incentives to researchers and entrepreneurs, and public-private partnerships to accelerate the uptake of research outputs by the industry.

Conclusions

Plant-based (botanical) pesticide products have historically been used and have the potential to manage plant diseases. Various active compounds have been isolated and identified from multiple effective formulations that can potentially manage plant diseases if used and applied in the correct doses. However, the development and utilization of these products face various challenges at various levels. Due to the need for safe and sustainable pest control products, biopesticides provide opportunities for the sector's growth. The government and policymakers should create an enabling regulatory environment to help facilitate sustainable value chains for commercialized botanical pest control products. Consumers can also promote investment in this area by developing a remunerative market segment that encourages the use of these products.

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