Alkaloid Role in Plant Defense Response to Growth and Stress

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Abstract

In the natural habitats, plants are surrounded by a different number of enemies, including a wide variety of viruses, bacteria, fungi, nematodes, insects, and other herbivorous, which are responsible for the deleterious reduction in plant growth and production. Plants protect themselves by producing a diverse array of compounds called secondary metabolites, including terpenes, phenolics, sulfur-containing compounds, saponins, and alkaloids. Alkaloids are a diverse group of nitrogen-containing basic natural products consisting of more than 20 different classes including pyrrolidines, pyrrolizidine, quinolizidine, tropanes, piperidines, pyridines, and others. Most alkaloids are believed to function as (1) storage reservoirs of nitrogen, (2) defensive elements against predators, especially animals, vertebrates, insects as well as arthropods due to their general toxicity and deterrence capability, and (3) growth regulators, since the structures of some alkaloids are similar to known plant growth regulators. In addition, a number of alkaloids are being used as a source of medicinal drugs for thousands of years due to their structure–activity relationship, and this line of interest is still a major one for organic chemistry and pharmaceutical industries. For example, quinine, which is derived from the bark of tropical cinchona tree, has been used by Indians of South America for fever treatment and later proved to be an

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essential remedy needed for malaria disease. Considerable efforts have been carried out in the biosynthesis pathways of alkaloids and their intermediate compounds. This chapter presents an overview of the recent studies on the role of alkaloids as specific plant protectants to pathogen attack and other damaging creatures. In addition, we critically evaluate the availability and significant of alkaloid's genetic resources with desirable biotic stress resistance traits.

Keywords
Alkaloids · Plant defense · Plant–pathogen interaction

9.1 Introduction

9.1.1 What are Alkaloids

Alkaloids are naturally occurring chemical compounds containing nitrogenous organic molecules. Alkaloid name refers to the word alkaline that was used to describe any nitrogen-containing base. Most organisms produced alkaloids, including bacteria, fungi, plants, and animals and considered an essential part of secondary metabolites (Matsuura and Fett-Neto 2015). Plant alkaloids are one of the largest groups of natural products represented by approximately 12,000 natural products. Alkaloid classification depends on the presence of a basic nitrogen atom at any position in the molecule, in which nitrogen does not include in peptide bond (Robinson 1974). Plant containing alkaloids have been used by different folks for approximately 300 decades in medicines and teas, but the active compounds were not isolated and identified until the nineteenth century, and its chemical nature and structure discovered have been reported recently. Since the isolation of alkaloids in nineteenth century, they are used in the medicine of alkaloid drugs. Through the history of alkaloids, opium was the first crude drug to be chemically investigated, that had been used as an analgesic and narcotic drug for many centuries. Opium alkaloids isolated for the first time in 1803 by Derosne, three years later Sertürner (1806) recognized the alkaline nature of the somniferous principle of opium, and after ten years he titled it as morphine. From 1817 to 1820, Pelletier and Caventou discovered an exciting series of active compounds, including caffeine from coffee, strychnine from nux-vomica, emetine from ipecac, quinine and cinchonine from cinchona bark, shortly after that followed by coniine. Currently, the advanced NMR techniques and X-ray diffraction spectrometry permit the explanation of most chemically complex structures. Most alkaloids that react with acids to form salts are characterized by the crystalline shape. In the plant, they may be formed as salts or as N-oxides. As alkaloids are essential active compounds, many attempts have been made recently to produce alkaloids in plant's tissue culture. Nowadays, about 30 alkaloid compounds are commercially interested especially in medicines,

flavorings, or poisons (Bribi 2018). In ancient time, plant alkaloids had been observed and used in ancient times but without any explanation. They have been used by man more than 3000 years ago for many purposes, for example, in Mesopotamia since 2000 BCE, medicinal plants Papaver somniferum and Atropa belladonna used in therapeutic purposes, Amanita muscaria used in ancient India (Aniszewski 2007).

9.2 Alkaloids Role in Plant Defense

9.2.1 Alkaloids as Anti-Pathogens

Plants accumulate antimicrobial secondary metabolites to protect themselves. Some of these metabolites are constitutive chemical barriers to microbial attack (phytoanticipins) and (phytoalexins) as inducible antimicrobials (González-Lamothe et al. 2009; Abdelrahman et al. 2014, 2017a, b). Plant alkaloids are one of the important secondary metabolites that play a crucial role in plant defense. Plant alkaloids have both blessing and curse of nature and have the ability to produce beneficial and toxic bioactive natural compounds (Cushnie et al. 2014). Alkaloids are one of the strategies that plants use in order to defend themselves against the great variety of potential environmental threats. One of the important danger causes of plant diseases is the biotic agents (including fungi and bacteria). Figure 9.1 shows the bioactivity of some plant alkaloids used in defense against certain pathogens. Pathogens establish a close connection with their hosts to suppress and prevent plant defenses and promote the nutrient release. Plants protect themselves from pathogens by a variety of incredible strategies among them the production of toxic compounds (Freeman and Beattie 2008). Any part of the plant could produce alkaloids, and specific compounds may be limited to a certain plant's part as quinine in *cinchona* tree bark (Robbers et al. 1996). Beside microorganisms as the common source of antibiotics, higher plants have also been a source of antibiotics. Examples from higher plants as antibiotic contacting plants, *Allium sativum* (garlic) has allinine alkaloid, an effective antibiotic, and berberine alkaloid extracted from goldenseal (*Hydrastis Canadensis*) has antimicrobial effects (Trease and Evans 1972). In the following part, we discuss the role of some alkaloids as antimicrobial agents from higher plants containing alkaloids. In Table 9.1, a list of the potential role of some plant alkaloid groups and compounds as anti-pathogens. Emetine alkaloid found in the underground part of *Cephaelis ipecacuanha* and related species used as an amoebicidal drug and used for the treatment of abscesses due to the spread of *Entamoeba histolytica* infections (Iwu et al. 1999). As demonstrated in plenty of studies, secondary metabolites play a crucial role in the ecology of plants and their survival and fitness; hence in the sweet and wild-type species of *Lupinus*, alkaloids play an important role in plant defense. De la Vega et al. (1996) investigated the role of lupanine, lupinine, and gramine alkaloidal antimicrobial effect against four bacterial types: *Pseudomonas syringae P.V. phaseolicola;*

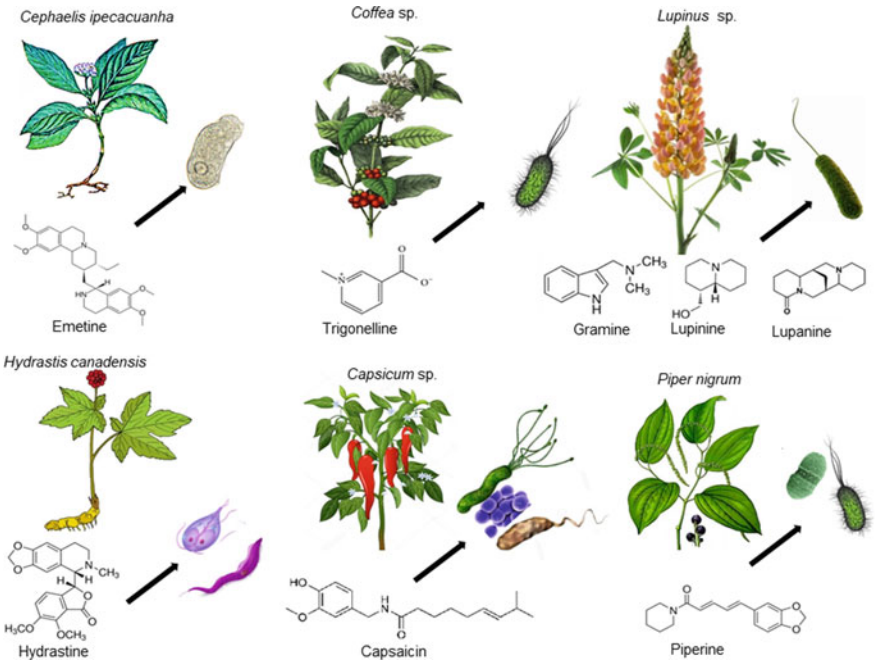

Fig. 9.1 Diagrammatic graph shows some plants and their related enemies and the role of alkaloids in defensive process

Table 9.1 Some alkaloid groups and compounds naturally occurring in plants and their defensive role in protection against pathogens

Alkaloids type	Plant species name	Pathogenic organisms	References
Lupanine, lupinine, and Gramine	*Lupinus albus (L.) and Lupinus luteus (L.)*	*Pseudomonas syringae P.V. phaseolicola; Pseudomonas syringae P.V. tomato; Pseudomonas putida; Erwinia carotovora var. carotovora*	de la Vega et al. (1996)
Quinolizidine	*Dictamnus dasycarpus*	*Erysiphe graminis*	Zhao et al. (1998)
Emetine	*Cephaelis ipecacuanha*	*Entamoeba histolytica*	Iwu et al. (1999)
α-tomatine	*Solanum lycopersicum*	*Fungi*	Eltayeb and Roddick (1984), Kozukue et al. (2004)

(continued)

Table 9.1 (continued)

Alkaloids type	Plant species name	Pathogenic organisms	References
7-demethoxytylophorine	*Cynanchum komarovii*	*Tobacco mosaic virus*	An et al. (2001)
Pyrrolizidine	*Heliotropium subulatum*	*Five bacteria, four fungi*	Singh et al. (2002)
7-deoxytransdihydronarciclasin	*Hosta plantaginea*	*Tobacco mosaic virus*	Wang et al. (2007)
Trigonelline	*Coffea*	*Escherichia coli, and Staphylococcus enterica*	López-Gresa et al. (2009), Almeida et al. (2006)
Naphthylisoquinoline	*Ancistrocladus abbreviatus, Triphyophyllum peltatum*	*Botrytis cinerea*	Aniszewski (2007)
β-carboline	*Picrasma quassioides*	*Tobacco mosaic virus*	Chen et al. (2009)
Berberines	*Hydrastis canadensis*	*Bacteria*	Ettefagh et al. (2011)
Protoberberine	*Radix Berberidis, Rhizoma coptidis and Cortex Phellodendri*	*Escherichia coli, Staphylococcus aureus, Shigella dysenteriae, Streptococcus pneumoniae and Candida albicans*	Qi et al. (2013)
Capsaicin	*Capsicum*	*Helicobacter pylori, Pseudomonas aeruginosa, Vibrio cholerae, Staphylococcus aureus, and Porphyromonas gingivalis*	Marini et al. (2015)
Ricinine and its derivatives	*Ricinus communis*	*Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and Candida albicans*	El-Naggar et al. (2017)
β-carbolines	*Peganum harmala*	*Staphylococcus aureus, Staphylococcus aureus, Escherichia coli, Candida albicans, Candida*	Suzuki et al. (2018)

(continued)

Table 9.1 (continued)

Alkaloids type	Plant species name	Pathogenic organisms	References
		intermedia, Candida krusei	
Cocaine	*Erythroxylum coca*	*Gram-negative and gram-positive cocci*	Tiku (2018)
Piperine	*Piper nigrum*	*Lactobacillus, Micrococcus, Escherichia coli, Enterococcus faecalis*	Tiku (2018)
Colchicine	*Gloriosa superba*	*Bacteria and fungi*	Tiku (2018)
Hydrastine	*Hydrastis canadensis*	*Bacteria, Giardia duodenalis, trypanosomes*	Tiku (2018)
Berberine	*Mahonia aquifolium*	*Plasmodium Trypanosomes, general*	Tiku (2018)
Reserpine	*Vinca minor*	*General*	Tiku (2018)
Mescaline	*Lophophora williamsii*	*General*	Tiku (2018)
Quinine	*Cinchona sp.*	*Plasmodium spp.*	Tiku (2018)
Reserpine	*Rauwolfia serpentina*	*General*	Tiku (2018)
Quinolizidine	*Vicia faba*	*Bacteria*	Tiku (2018)
Oleuropein glucoside	*Solanum nigrum*	*Fungi*	Tiku (2018)
Veremivirine	*Solanum nigrum*	*Fungi*	Tiku (2018)
Myristic acid	*Solanum nigrum*	*Fungi*	Tiku (2018)
Nicotine	*Tobacco*	*Bacteria and fungi*	Tiku (2018)
Berberine	*Berberis vulgaris*	*Bacteria and protozoa*	González-Lamothe et al. (2009), Tiku (2018)
6 indole alkaloids	*Kopsia genus*	*Bacteria and fungi*	Long et al. (2018)

Pseudomonas syringae P.V. tomato; Pseudomonas putida; Erwinia carotovora var. carotovora. Lupinine was the most effective bactericidal agent against the four studied bacteria while gramine was effective controller agent of *P: phaseolicola and P: tomato* (de la Vega et al. 1996). An α-tomatine alkaloid extracted from most organs of *Solanum lycopersicum* have antifungal activity as reported by Eltayeb and Roddick (1984), Kozukue et al. (2004). An et al. (2001) studied two alkaloids 7-demethoxytylophorine and 7-demethoxytylophorine from *Cynanchum komarovii* have antiviral activity against TMV ranging from 60% to 65% at a concentration of 500 and 10 μg/mL. Several angiosperm species produce nitrogen-based secondary metabolites PAs (pyrrolizidine) alkaloids. Pyrrolizidine alkaloids (PAs) are quite

toxic and help in defense against infection caused by microbes. *Heliotropium subulatum* contains five pyrrolizidine alkaloids that have antimicrobial activity against many bacteria and fungi (Singh et al. 2002). Tobacco mosaic virus (TMV) is one of the most ancient and threatening viruses for tobacco, pepper, cucumber, and ornamental crops resulting in gigantic economic losses. Many studies attempted to solve the TMV virus crisis by eco-friendly approaches using naturally occurring secondary metabolites. 7-deoxytransdihydronarciclasin alkaloid was extracted and separated from *Hosta plantaginea* exhibited anti-TMV activity (Wang et al. 2007). Trigonelline alkaloid was firstly isolated by Jahns from the seeds of *Trigonella foenum-graecum* species belong to Leguminosae, widely cultivated in India and Egypt. Trigonelline is an alkaloid extracted from coffee that has an antibacterial effect on *Escherichia coli* and *Salmonella enterica* (López-Gresa et al. 2009; Almeida et al. 2006). Naphthylisoquinoline alkaloids extracted from tropical lianas *Ancistrocladus abbreviatus* and *Triphyophyllum peltatum* inhibit the growth of *Botrytis cinerea* fungus (Aniszewski 2007). Chen et al. (2009) used β-carboline alkaloids and a quassinoid from the *Picrasma quassioides* wood as antiviral against TMV exhibited positive results. Ettefagh et al. (2011) extracted alkaloids from roots and shoots of *H. canadensis,* but they found that the higher concentration was in roots especially berberine followed by hydrastine and canadine was the lowest. Protoberberine alkaloids extracted from three medicinal plants *Radix Berberidis, Rhizoma coptidis,* and *Cortex Phellodendri* have antimicrobial activity against *E. coli, Staphylococcus aureus, Shigella dysenteriae, Streptococcus pneumoniae,* and *Candida albicans,* where *Rhizoma coptidis* has the strongest antimicrobial activities (Qi et al. 2013). The antimicrobial and anti-virulence activity of capsaicin recently had considerable attention. Capsaicin has an antibacterial effect against food-borne pathogens, *Helicobacter pylori*, and *Pseudomonas aeruginosa* and has anti-virulence activity against *Vibrio cholerae*, *S. aureus*, and *Porphyromonas gingivalis* (Marini et al. 2015). El-Naggar et al. (2017) studied and proved the antimicrobial activity of ricinine on bacterial and fungal species as follows: *S. aureus, E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and C. albicans.* β-carbolines constitute a large group of indole alkaloids and are distributed widely in different types of organisms among them plants. Plants contain simple β-carboline called harmala alkaloids and were firstly discovered form *Peganum harmala* L. (Zygophyllaceae), which is being used as a traditional medicine in the Middle East and North Africa. The effect of quaternary ammonium groups in antibacterial agents causes the forthwith death of the bacterial cell by disrupting negatively charged bacterial cell membrane followed by the release of K^+ ions and other cytoplasmic constituents (Suzuki et al. 2018). Suzuki et al. (2018) were reported the antimicrobial effects of β-carboline derivatives against bacteria and fungi: *S. aureus, S. aureus, E. coli, C. albicans, Candida intermedia, Candida krusei*; they concluded the possibility of the synthesis of naturally occurring β-carboline derivatives and their N2—alkylated analogs. Tiku (2018) reported many plants as a source for many antimicrobial alkaloids. For example, cocaine alkaloid found in *Erythroxylum coca* is effective against gram-negative and gram-positive cocci. Piperine, an antibacterial and antifungal

alkaloid formed by *Piper nigrum,* has antimicrobial effects against *Lactobacillus* sp., *Micrococcus* sp., *Escherichia coli, E. faecali.* Long et al. (2018) studied the antimicrobial effect of six alkaloids extracted from *Kopsia fruticosa* areal parts against two gram-positive bacteria and five gram-negative bacteria, and antifungal activities against five pathogens.

9.2.2 Alkaloids Toxicity to Insects

Plants have designed strong strategies to detect and defend themselves against invading organisms before causing extensive damage. As plants are the main vital food source for human, so we need to protect our food supply and develop highly disease-resistant plant species, and we should understand how plants defend themselves from pathogens and herbivores. Most alkaloids are toxic to some degree and play a primary role in plant defense against microbial infection and herbivore attack. Plant alkaloids have major role described in many scientific literatures as protecting agents against herbivores because alkaloids have special characteristics such as bitter flavor, disruption of protein activity after ingestion and metabolization, and central nervous system alteration (Matsuura and Fett-Neto 2015). Table 9.2 shows the effective role of some plant alkaloids defense against selected

Table 9.2 Plant alkaloid groups and compounds and their protective relation against insects

Alkaloids type	Plant species name	Insect	References
Quinolizidine	*Lupinus sp.*	*Insects*	Keeler (1989)
Ricinine	*Ricinus communis*	*Atta sexdens rubropilosa*	Bigi et al. (2004)
Naphthylisoquinoline	*Ancistrocladus abbreviatus* and *Triphyophyllum peltatum*	*Spodoptera littoralis*	Aniszewski (2007)
Harmine derivatives	*Peganum harmala*	*Mosquitos, mustard aphid*	Zeng et al. (2010)
Colchicine	*Colchicum autumnale*	*Apis mellifera*	Mithöfer and Boland (2012)
Alkaloidal extract	*Pergularia tomentosa*	*Locusta migratoria cinerascens*	Acheuk and Doumandji-Mitiche (2013)
Demissine	*Solanum demissum*	*Leptinotarsa decemlineata and Empoasca fabae*	Fürstenberg-Hägg et al. (2013)
Caffeine	*Coffea arabica*	*Coffea feeding insects*	Matsuura and Fett-Neto (2015)
Antofine N-oxide	*Cynanchum mongolicum*	*Spodoptera litura*	Ge et al. (2015)

(continued)

Table 9.2 (continued)

Alkaloids type	Plant species name	Insect	References
Antofine	*C. mongolicum*	*Lipaphis*	Ge et al. (2015)
Chili pepper extract	*Capsicum frutescens*	*Coptotermes gestroi*	Colon et al. (2016)
Pellitorine	*Zanthoxylum piperitum*	*Culex pipiens pallens and Aedes aegypti*	Kim and Ahn (2017)
Ricinine	*Ricinus communis*	*Atta sexdens*	Santos et al. (2018)
Amabiline	*Lycoris radiate*	*Aphis citricola*	Yan et al. (2018)
Deoxydihydrotazettine	*L. radiate*	*A. citricola*	Yan et al. (2018)
Deoxytazettine	*L. radiate*	*A. citricola*	Yan et al. (2018)
3-epimacronine	*L. radiate*	*A. citricola*	Yan et al. (2018)
Galanthamine	*L. radiate*	*A. citricola*	Yan et al. (2018)
11-hydroxygalanthamine	*L. radiate*	*A. citricola*	Yan et al. (2018)
N-allylnorgalanthamine	*L. radiate*	*A. citricola*	Yan et al. (2018)
11β-hydroxygalanthamine	*L. radiate*	*A. citricola*	Yan et al. (2018)
Lycorine	*L. radiate*	*A. citricola*	Yan et al. (2018)
Colchicine	*L. radiate*	*A. citricola*	Yan et al. (2018)
Alkaloidal extract	*Catalpa ovata*	*Mythimna separata and Plutella xylostella*	Shao et al. (2018)

insects. Quinolizidine alkaloids constitute 5% of lupin seeds, which are toxic to insects as reported by Keeler (1989). Aphids are one of the pests most economically destructive of plants that transmit plant viruses and in turn leading to fungal infection causing a negative effect on photosynthesis by ingesting plant juices with their stylets and secreting honeydew, hence severe economic financial losses worldwide appear (Yan et al. 2018). Aphids are small sap-sucking insects which infest several economical important vegetable and fruit crops in different countries, including apple (*Malus domestica*), crab apple (*Malus sylvestris*), and papaya (*Carica papaya*). Yan et al. (2018) investigated the insecticidal effect of ten alkaloids including amabiline, deoxytazettine, deoxydihydrotazettine, 3-epimacronine, galanthamine, 11-hydroxygalanthamine, N-allylnorgalanthamine, 11β-hydroxygalanthamine, lycorine, and colchicine which are extracted from *Lycoris radiate* against *Aphis citricola.* Among all tested alkaloids, the first nine compounds exhibited a potential aphicidal activity against *A. citricola.* N-allylnorgalanthamine showed the best inhibitory effect as aphicidal in both *in vivo* and *in vitro* against *A. citricola.* Ricinine alkaloid has been found in all parts of *Ricinus communis* plant and has insecticidal activity against *Atta sexdens* (Santos et al. 2018). *A. abbreviatus* and *T. peltatum* plant species have naphthylisoquinoline alkaloid with insecticidal effects on *Spodoptera littoralis* (Aniszewski 2007). *Colchicum*

autumnal, family Colchicaceae produced Colchicine alkaloid which have many harmful effects to honey bee (Apis mellifera). Colchicine alkaloid is toxic and inhibits microtubule polymerization by binding to tubulin and inhibiting mitosis (Mithöfer and Boland 2012). Caffeine, present in *Coffea arabica* and various other plant species is toxic and paralyzes insects feeding on the plant as it inhibits phosphodiesterase activity and promotes an increase in intracellular cyclic AMP level (Matsuura and Fett-Neto 2015). *Cynanchum mongolicum* contains three insecticidal alkaloids: antofine N-oxide, antofine, and tylophorine as identified by Ge et al. (2015). Antofine has the highest toxicity, and the three alkaloids have significant toxicity against aphid *Lipaphis erysimi*. Most of the alkaloids secreted by plants have potent effects on insect pests; hence, these botanical nature organic molecules provide a safe source of pesticides compounds that are eco-friendly. *Pergularia tomentosa* alkaloids extracted from shoot parts had a considerable larvicidal effect on *Locusta migratoria cinerascens* (Acheuk and Doumandji-Mitiche 2013). Chili pepper (sizzling taste) has many nutritional benefits like a source for vitamin A and C, and it also has the capability to kill household insects. Capsaicin is the dominant compound found in the many varieties of chilies with other compounds. Fruit extract of *Capsicum frutescens* prepared by Colon et al. (2016) is an insecticide against household termites. Harmine derivative compounds found in medicinal plants such as *P. harmala* are active insecticide as demonstrated by (Zeng et al. 2010) against *Culex pipiens quinquefasciatus* and *L. erysimi,* compounds 1-phenyl-1,2,3,4-tetrahydro-β-carboline-3-carboxylic acid, and methyl 1-phenyl-β-carboline-3-carboxylate had an insecticidal effect in both *in vitro* and *in vivo*. Three different concentrations of the total alkaloids extracted from the root bark of *Catalpa ovata* were used to investigate the insecticide activity against *Plutella xylostella,* and *Oriental armyworm* and the findings exhibited positive result as a potential insecticide (Shao et al. 2018). *Zanthoxylum piperitum* bark contains pellitorine alkaloid which is very toxic to third-instar larvae of *Mythimna separata* and *Plutella xylostella* as demonstrated by (Kim and Ahn 2017). Ricinine alkaloid extracted from *R. communis* causes the death of leaf-cutting ant (*Atta sexdens rubropilosa*) (Bigi et al. 2004). Nightshade potato (*Solanum demissum*) contains demissine alkaloid characterized by its resistant to Colorado beetle (*Leptinotarsa decemlineata*) and potato leafhopper (*Empoasca fabae*) (Fürstenberg-Hägg et al. 2013).

9.2.3 Alkaloids as Deterrents

Deterrent alkaloids play an important role as mediators in insect–plant interactions, as they are unpalatable by many herbivorous insects (Shields et al. 2008). Recently, most alkaloids are believed to play a crucial role as defensive agents against predators, especially mammals because of their toxicity and deterrence capability (Mazid et al. 2011). Most of the alkaloids occur in higher plants with 20–30% and are mostly found in dicotyledonous angiosperms with concentrations of about more than 0.01% of the dry weight (Shields et al. 2008). Livestock death disaster is

caused by the ingestion of alkaloid-containing plants. For example, in the USA, huge percentage of all grazing livestock are poisoned and lost yearly by feeding on large quantities of alkaloid-containing plants such as lupines (*Lupinus* sp.) and larkspur (*Delphinium* sp.). Alkaloid's effects in animal cells are varied as follow, may interfere with nervous system components especially the chemical transmitters, affect membrane transport, protein synthesis and activities of the miscellaneous enzymes (Mazid et al. 2011). Nine alkaloids (acridine, aristolochic acid, atropine, berberine, caffeine, nicotine, scopolamine, sparteine, and strychnine) were investigated for their feeding deterrent behavior on gypsy moth larvae, and the result was those feeding deterrent responses for all the alkaloids tested depend on alkaloid concentration. Berberine and aristolochic acid were the most potent antifeedants comparing with other tested alkaloids (Shields et al. 2008). Nicotine and capsaicin alkaloids have decreased feeding effects when applying *Henosepilachna viginti octomaculata* to Motsch (Chowanski et al. 2016). *P. tomentosa* alkaloids extracted by Acheuk and Doumandji-Mitiche (2013) mentioned above as insecticidal against larvae of *Locusta migratoria cinerascens* and also have anti-feeding effect causing weight loss of these larvae (Acheuk and Doumandji-Mitiche 2013).

9.2.4 Allelopathic Activity of Alkaloids

Although there are great contribution of alkaloids as allelopathy but little reports dealt with alkaloids involved in allelopathy: for example: alkaloids of *Datura stramonium* inhibited the germination of many crop species, and the role of lupin alkaloids in inhibition of seed germination. Of other alkaloids reported to have allelopathic activity, cocaine from *Erythroxylon* coca Lamk (coca) (Roberts and Wink 1998). Berberine, sanguinarine, and gramine alkaloids inhibited the seedling growth of *Lactuca sativa* and *Lepidium sativum* as recorded by (Matsuura and Fett-Neto 2015). Alkaloids such as quinine, cinchonidine, nicotine, boldine, lobeline, coniine, and harmaline manifested harmful phytotoxic effects to *Lemna gibba* causing cell chlorosis or death (Matsuura and Fett-Neto 2015).

9.3 Conclusion

Plants have developed multiple defense strategies against microbial infections and various types of environmental stress. Natural alkaloids obtained from plants play an important role in plant disease prevention and promoting healthcare world-wide. Alkaloids offer a diverse range of structurally unique bioactive molecules, which have been used as a significant source of useful and innovative therapeutic agents. An in-depth study on metabolic efficacy, transformation, and safety of alkaloids will accelerate their plant natural resource utilization and development. Furthermore, studies in the field of the regulation of the biosynthesis of terpenoid indole alkaloids on the level of genes and enzymes, and the feasible to clone these genes in

various plants might eventually lead to generate gene cassettes for complete pathways, which could then be used for production of valuable defensive secondary metabolites in transgenic plants or plant cell cultures with improved productivity of the desired compounds. In addition, the recent emergence of liquid chromatography–mass spectrometry will facilitate the isolation, identification, and quantification processes of different alkaloids. This revolution in mass spectrometry has significantly enabled us to generate several metabolic databases (e.g., https://www.genome.jp/kegg/pathway.html, https://metacyc.org/ and others) which can provide an in-depth insight regarding plant–pathogen interaction. Thus, the biological screening of new active alkaloids, using a wide variety of robust tools and the interactive collaboration of experts in diverse scientific disciplines in connection with studies on the role of secondary metabolism for plants, may contribute to a better understanding of resistance of plants to diseases and various herbivores.

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